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(54) Title: GENE EXPRESSION PROFILES IN NORMAL AND CANCER CELLS (57) Abstract As a step towards understanding the complex differences between normal and cancer cells, gene expression patterns were examined in gastrointestinal tumors. More than 300,000 transcripts derived from at least 45,000 different genes were analyzed. Although extensive similarity was noted between the expression profiles, more than 500 transcripts that were expressed at significantly different levels in normal and neoplastic cells were identified. These data provide insights into the extent of expression differences underlying malignancy and reveal genes that are useful as diagnostic or prognostic markers.		

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Gene Expression Profiles in Normal and Cancer Cells

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TECHNICAL FIELD OF THE INVENTION

This invention is related to the diagnosis of cancer, and tools for carrying out such diagnosis.

BACKGROUND OF THE INVENTION

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Much of cancer research over the past 50 years has been devoted to the analyses of genes that are expressed differently in tumor cells compared to their normal counterparts. Although hundreds of studies have pointed out differences in the expression of one or a few genes, no comprehensive study of gene expression in the cancer cell has been reported. It is therefore not known how many genes are expressed differentially in tumor versus normal cells, whether the bulk of these differences are cell autonomous rather than being dependent on the tumor microenvironment, and whether most differences are cell-type specific or tumor specific. Thus there is a need in the art for information on the molecular changes that occur in cells during cancer development and progression.

SUMMARY OF THE INVENTION

According to one embodiment of the invention, a method is provided for diagnosing colon cancer in a sample suspected of being neoplastic. The method comprises the steps of:

5 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 3;

10 identifying the first sample as neoplastic when the level of the at least one transcript is found to be lower in the first sample than in the second sample.

According to another embodiment of the invention, another method is provided for diagnosing colon cancer in a sample suspected of being neoplastic.

15 The method comprises the steps of:

 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 2;

20 identifying the first sample as neoplastic when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

25 In another embodiment of the invention an isolated and purified human nucleic acid molecule is provided. The molecule comprises a SAGE tag selected from SEQ ID NO:1-732.

30 In yet another aspect of the invention an isolated nucleotide probe is provided. The probe comprises at least 12 nucleotides of a human nucleic acid molecule, wherein the human nucleic acid molecule comprises a SAGE tag selected from SEQ ID NO: 1-732.

According to another aspect of the invention a method is provided for diagnosing pancreatic cancer in a sample suspected of being neoplastic. The method comprises the steps of:

5 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a pancreatic tissue suspected of being neoplastic and the second sample is of a normal human colon tissue, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 4;

10 identifying the first sample as neoplastic when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

According to still another embodiment of the invention a method of diagnosing cancer in a sample suspected of being neoplastic is provided. The method comprises the steps of:

15 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a tissue suspected of being neoplastic and the second sample is of a normal human tissue, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 5;

20 identifying the first sample as neoplastic when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

According to another embodiment of the invention a method is provided to aid in the determination of a prognosis for a colon cancer patient.

25 The method comprises the steps of:

 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic colonic tissue and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 3;

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determining a poorer prognosis if the level of the at least one transcript is found to be lower in the first sample than in the second sample.

According to another aspect of the invention a method to aid in determining a prognosis for a patient with colon cancer is provided. The method comprises the steps of:

comparing the level of at least one transcript in a first tissue sample to a second sample, wherein the first sample is of a colonic cancer tissue and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 2;

determining a poorer prognosis if the level of the at least one transcript is found to be higher in the first sample than in the second sample.

In yet another embodiment of the invention a method is provided for diagnosing colon cancer in a sample suspected of being neoplastic. The method comprises the steps of:

comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 3;

identifying the first sample as neoplastic when the level of expression of the protein is found to be lower in the first sample than in the second sample.

In another aspect of the invention a method of diagnosing colon cancer in a sample suspected of being neoplastic is provided. The method comprises the steps of:

comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript

identified by a tag selected from the group consisting of those shown in Table 2;

identifying the first sample as neoplastic when expression of the protein is found to be higher in the first sample than in the second sample.

5 According to another embodiment of the invention a method is provided to aid in determining a prognosis of a patient having pancreatic cancer. The method comprises the steps of:

 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic pancreatic tissue and the second sample is of a normal human colon tissue, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 4;

 determining a poorer prognosis if transcription is found to be higher in the first sample than in the second sample.

15 In yet another aspect of the invention a method to aid in providing a prognosis for a cancer patient is provided. The method comprises the steps of:

 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic tissue and the second sample is of a normal human tissue of the same tissue type, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 5;

20 determining a poorer prognosis if transcription is found to be higher in the first sample than in the second sample.

 According to still another aspect of the invention, a method is provided for diagnosing pancreatic cancer in a sample suspected of being neoplastic. The method comprises the steps of:

 comparing the level of expression of at least one protein encoded by a transcript in a first sample of a tissue to a second sample, wherein the first sample is of a pancreatic tissue suspected of being neoplastic and the second sample is of a normal human colon tissue, wherein said protein is

encoded by a transcript identified by a tag selected from the group consisting of those shown Table 4;

identifying the first sample as neoplastic when expression of the protein is found to be higher in the first sample than in the second sample.

5 According to yet another aspect of the invention a method is provided for diagnosing cancer in a sample suspected of being neoplastic. The method comprises the steps of:

10 comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a tissue suspected of being neoplastic and the second sample is of a normal human tissue, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 5;

identifying the first sample as neoplastic when expression of the protein is found to be higher in the first sample than in the second sample.

15 In still another embodiment of the invention a method is provided to aid in the determination of a prognosis of a colon cancer patient. The method comprises the steps of:

20 comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic colonic tissue and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 3;

determining a poorer prognosis if the level of expression is found to be lower in the first sample than in the second sample.

25 In still another embodiment of the invention a method is provided to aid in determining a prognosis for a patient with colon cancer. The method comprises the steps of:

30 comparing the level of expression of at least one protein in a first tissue sample to a second sample, wherein the first sample is of a colonic cancer tissue and the second sample is of a normal human colonic tissue, and

wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 2;

determining a poorer prognosis if the level of expression is found to be higher in the first sample than in the second sample.

5 In still another aspect of the invention a method is provided to aid in determining a prognosis of a patient having pancreatic cancer. The method comprises the steps of:

10 comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic pancreatic tissue and the second sample is of a normal human colon tissue, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 4;

determining a poorer prognosis if the level of expression is found to be higher in the first sample than in the second sample.

15 According to even a further aspect of the invention a method is provided to aid in providing a prognosis for a cancer patient. The method comprises the steps of:

20 comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic tissue and the second sample is of a normal human tissue of the same tissue type, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 5;

determining a poorer prognosis if the level of expression is found to be higher in the first sample than in the second sample.

25 In still another embodiment of the invention a method of treating a cancer cell is provided. The method comprises the step of:

30 administering to a cancer cell an antibody which specifically binds to a protein encoded by a transcript identified by a tag selected from the group consisting of those shown in Tables 2, 4, and 5, wherein the antibody is linked to a cytotoxic agent.

In another aspect of the invention an antibody linked to a cytotoxic agent is provided. The antibody specifically binds to a protein encoded by a transcript identified by a tag selected from the group consisting of those shown in Tables 2, 4, and 5.

5 According to another aspect of the invention, a method of detecting colon cancer in a patient is provided. The method comprises the steps of:

 comparing the level of at least one protein or transcript in a first body sample to a second body sample, wherein the first sample is a body sample of the patient and the second sample is of a normal human, wherein the
10 protein is encoded by a transcript and the transcript is identified by a tag selected from the group consisting of those shown in Table 2, wherein the first and second body sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

 identifying neoplasia when the level of the at least one protein
15 or transcript is found to be higher in the first sample than in the second sample.

In another aspect of the invention a method of detecting pancreatic cancer in a patient is provided. The method comprises the steps of:

 comparing the level of at least one protein or transcript encoded by a transcript in a first sample of a tissue to a second sample, wherein the first
20 sample is of the patient and the second sample is of a normal human, wherein said protein is encoded by a transcript and the transcript is identified by a tag selected from the group consisting of those shown Table 4, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

25 identifying neoplasia when the level of the at least one protein or transcript is found to be higher in the first sample than in the second sample.

Also provided by the present invention is a method of detecting cancer in a patient. The method comprises the steps of:

30 comparing the level of at least one protein or transcript in a first sample to a second sample, wherein the first sample is of patient and the second sample is of a normal human, wherein said protein is encoded by a

transcript and the transcript is identified by a tag selected from the group consisting of those shown Table 5, wherein the first and second body sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

5 identifying neoplasia when the level of the at least one protein or transcript is found to be higher in the first sample than in the second sample.

Additionally provided by the present invention is a method to aid in the determination of a prognosis for a colon cancer patient. The method comprises the steps of:

10 comparing the level of at least one protein or transcript in a first sample to a second sample, wherein the first sample is of a colon cancer patient and the second sample is of a normal human, wherein the protein is encoded by a transcript and the transcript is identified by a tag selected from the group consisting of those shown in Table 3, wherein the first and second body sample
15 is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

determining a poorer prognosis if the level of the at least one protein or transcript is found to be lower in the first sample than in the second sample.

20 Provided by another embodiment of the invention is a method to aid in determining a prognosis for a patient with colon cancer. The method comprises the steps of:

comparing the level of at least one protein or transcript in a first sample to a second sample, wherein the first sample is of a colonic cancer patient and the second sample is of a normal human, wherein the protein is encoded by a transcript and the transcript is identified by a tag selected from the group consisting of those shown in Table 2, wherein the first and second
25 sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

determining a poorer prognosis if the level of the at least one protein or transcript is found to be higher in the first sample than in the second sample.

5 According to still another aspect of the invention, a method to aid in determining a prognosis of a patient having pancreatic cancer is provided. The method comprises the steps of:

10 comparing the level of at least one protein or transcript in a first sample to a second sample, wherein the first sample is of a pancreatic cancer patient and the second sample is of a normal human, wherein said protein is encoded by a transcript and the transcript is identified by a tag selected from the group consisting of those shown Table 4, wherein said first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

15 determining a poorer prognosis if the level of the at least one protein or transcript is found to be higher in the first sample than in the second sample.

Also provided by the present invention is a method to aid in providing a prognosis for a cancer patient. The method comprises the steps of:

20 comparing the level of expression of at least one protein or transcript in a first sample to a second sample, wherein the first sample is of a cancer patient and the second sample is of a normal human, wherein said protein is encoded by a transcript and the transcript is identified by a tag selected from the group consisting of those shown Table 5, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

25 determining a poorer prognosis if the level of the at least one protein or transcript is found to be higher in the first sample than in the second sample.

30 The present invention further includes antisense oligonucleotides complementary in whole or in part to SEQ ID NOS:1-732.

This invention also provides a method for screening for candidate agents that modulate the expression of a polynucleotide selected from the group consisting of the polynucleotides in SEQ ID NOS.1-732 or their respective complements, by contacting a test agent with a pancreatic or colon cell and monitoring expression of the polynucleotide, wherein the test agent which

5 modifies the expression of the polynucleotide is a candidate agent.

The present invention provides the art with new methods and reagents for diagnosing and prognosing cancers. In addition, some of the newly disclosed genes may play an important role in the development of cancers.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1. Comparison of expression patterns in colorectal cancers and normal colon epithelium. **(FIG. 1A)** A semi-logarithmic plot reveals 51 tags that were decreased more than 10 fold in primary CR cancer cells whereas 32 tags were increased more than 10 fold. 62,168 and 60,878 tags derived from normal colon epithelium and primary CR cancers, respectively, were used for

15 this analysis. The relative expression of each transcript was determined by dividing the number of tags observed in tumor and normal tissue as indicated. To avoid division by 0, a tag value of 1 was used for any tag that was not detectable in one of the samples. These ratios were then rounded to the nearest integer and their distribution plotted on the abscissa. The number of genes displaying each ratio was plotted on the ordinate. Tu: CR tumors; NC: Normal colon. **(FIG. 1B and FIG. 1C)** Differentially expressed genes in colorectal cancers. The number of transcripts found to be differentially expressed ($P < 0.01$) are presented as Venn diagrams. Diagrams of transcripts that were decreased **(FIG. 1B)** or increased **(FIG. 1C)** in CR cancers compared to normal colon epithelium. Comparisons were between primary tumors and cells in culture as indicated.

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Fig. 2. Northern blot analysis of genes differentially expressed in gastrointestinal neoplasia. Northern blot analysis was performed on total RNA (5 μ g isolated from primary CR carcinomas (T) and matching normal colon epithelium (N), or pancreatic carcinomas. The top panel in each case show an

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example of the ethidium bromide stained gels prior to transfer. The number of SAGE tags observed in the original analysis is indicated to the right of each blot. (FIG. 2A) Examples of transcripts that were decreased or increased in CR cancers. (FIG. 2B) Examples of transcripts increased in pancreatic cancers (10). (FIG. 2C) Examples of transcripts elevated in cancer which were or were not cancer type specific. Probes used for Northern blot analysis were as follows (Human SAGE Tag unique identifier, gene name, (GenBank accession number)): (FIG. 2A) H204104, Guanylin (M95714); H259108, (see Table 2); H1000193, (see Table 2); H998030, (see Table 2). (FIG. 2B) H294155, RIG-E (U42376); H560056, TIMP-1 (S68252). (FIG. 2C) H802810, EST338411 (W52120); H85882, 1-8D (X57351); H618841, GA733-1 (X13425).

Tables 2-5. Transcripts Differentially Expressed in Human Cancer.

Tag sequence represents the NlaIII site plus the adjacent 11 bp SAGE tag.

Tag number indicates a SAGE UID (unique identifier). NC, TU, CL, PT, PC, refers to the number of the indicated tag observed in RNA isolated from normal colorectal epithelium, primary colorectal cancers, colorectal cancer cell lines, primary pancreatic cancers, or pancreatic cancer cell lines, respectively. The Accession and Gene Name refer to representative GenBank entries that contain the tag sequence.

Table 2 Transcripts increased in colorectal cancer.

Table 3 Transcripts decreased in colorectal cancer.

Table 4 Transcripts increased in pancreatic cancer.

Table 5 Transcripts increased in pancreatic and colorectal cancer.

DETAILED DESCRIPTION

The inventors have discovered sets of human genes which are either upregulated or downregulated in cancer cells, as compared to normal cells. Specifically, certain genes have been found to be upregulated or downregulated in colorectal and/or pancreatic cancer cells, when compared to normal colon

cells. These sets of differentially regulated genes can be used as diagnostic markers, either individually or in sets of, for example, 2, 5, 10, 20, or 30.

Genes whose expression was detected to be increased in colorectal cancer are shown in Table 2. Genes whose expression was detected to be decreased in colorectal cancer are shown in Table 3. Genes whose expression was detected as increased in pancreatic cancer are shown in Table 4. Genes whose expression was detected as increased in both pancreatic cancer and colorectal cancer are shown in Table 5. These latter genes likely play a role in neoplastic development generally.

Tag sequences, as provided herein, uniquely identify genes. This is due to their length, and their specific location (3') in a gene from which they are drawn. The full length genes can be identified by matching the tag to a gene data base member, or by using the tag sequences as probes to physically isolate previously unidentified genes from cDNA libraries. The methods by which genes are isolated from libraries using DNA probes are well known in the art. See, for example, Veculescu et al., *Science* 270: 484 (1995), and Sambrook et al. (1989), *MOLECULAR CLONING: A LABORATORY MANUAL*, 2nd ed. (Cold Spring Harbor Press, Cold Spring Harbor, New York). Once a gene or transcript has been identified, either by matching to a data base entry, or by physically hybridizing to a cDNA molecule, the position of the hybridizing or matching region in the transcript can be determined. If the tag sequence is not in the 3' end, immediately adjacent to the restriction enzyme used to generate the SAGE tags, then a spurious match may have been made. Confirmation of the identity of a SAGE tag can be made by comparing transcription levels of the tag to that of the identified gene in certain cell types.

In addition to the sequences shown in SEQ ID NOS: 1-732, or their complements, this invention also provides the anti-sense polynucleotide stand, e.g. antisense RNA to these sequences or their complements. One can obtain an antisense RNA using the sequences provided in SEQ ID NOS: 1-732 and the methodology described in Vander Krol et al. (1988) *BioTechniques* 6:958.

The invention also encompasses polynucleotides which differ from that of the polynucleotides described above, but which produce the same phenotypic effect, such as the allele. These altered, but phenotypically equivalent polynucleotides are referred to "equivalent nucleic acids." This invention also encompasses polynucleotides characterized by changes in non-coding regions that do not alter the phenotype of the polypeptide produced therefrom when compared to the polynucleotide herein. This invention further encompasses polynucleotides, which hybridize to the polynucleotides of the subject invention under conditions of moderate or high stringency.

The polynucleotides can be conjugated to a detectable marker, e.g., an enzymatic label or a radioisotope for detection of nucleic acid and/or expression of the gene in a cell. A wide variety of appropriate detectable markers are known in the art, including fluorescent, radioactive, enzymatic or other ligands, such as avidin/biotin, which are capable of giving a detectable signal. In preferred embodiments, one will likely desire to employ a fluorescent label or an enzyme tag, such as urease, alkaline phosphatase or peroxidase, instead of radioactive or other environmental undesirable reagents. In the case of enzyme tags, colorimetric indicator substrates are known which can be employed to provide a means visible to the human eye or spectrophotometrically, to identify specific hybridization with complementary nucleic acid-containing samples. Briefly, this invention further provides a method for detecting a single-stranded polynucleotide identified by SEQ ID NOS.1-732 or its complement, by contacting target single-stranded polynucleotides with a labeled, single-stranded polynucleotide (a probe) which is at least 10 nucleotides of the complement of SEQ ID NOS: 1-732 (or the corresponding complement) under conditions permitting hybridization (preferably moderately stringent hybridization conditions) of complementary single-stranded polynucleotides, or more preferably, under highly stringent hybridization conditions. Hybridized polynucleotide pairs are separated from un-hybridized, single-stranded polynucleotides. The hybridized polynucleotide

pairs are detected using methods well known to those of skill in the art and set forth, for example, in Sambrook et al. (1989) *supra*.

5 The polynucleotides of this invention can be isolated using the technique described in the experimental section or replicated using PCR. The PCR technology is the subject matter of United States Patent Nos. 4,683,195, 4,800,159, 4,754,065, and 4,683,202 and described in PCR: The Polymerase Chain Reaction (Mullis et al. eds, Birkhauser Press, Boston (1994)) or MacPherson et al. (1991) and (1994), *supra*, and references cited therein. Alternatively, one of skill in the art can use the sequences provided herein and
10 a commercial DNA synthesizer to replicate the DNA. Accordingly, this invention also provides a process for obtaining the polynucleotides of this invention by providing the linear sequence of the polynucleotide, nucleotides, appropriate primer molecules, chemicals such as enzymes and instructions for their replication and chemically replicating or linking the nucleotides in the proper orientation to obtain the polynucleotides. In a separate embodiment, these polynucleotides are further isolated. Still further, one of skill in the art can insert the polynucleotide into a suitable replication vector and insert the vector into a suitable host cell (procaryotic or eucaryotic) for replication and amplification. The DNA so amplified can be isolated from the cell by methods
15 well known to those of skill in the art. A process for obtaining polynucleotides by this method is further provided herein as well as the polynucleotides so obtained.

RNA can be obtained by first inserting a DNA polynucleotide into a suitable host cell. The DNA can be inserted by any appropriate method, e.g.,
25 by the use of an appropriate gene delivery vector or by electroporation. When the cell replicates and the DNA is transcribed into RNA; the RNA can then be isolated using methods well known to those of skill in the art, for example, as set forth in Sambrook et al. (1989) *supra*. For instance, mRNA can be isolated using various lytic enzymes or chemical solutions according to the procedures set forth in Sambrook et al. (1989), *supra* or extracted by nucleic-acid-binding
30 resins following the accompanying instructions provided by manufactures.

Polynucleotides having at least 10 nucleotides and exhibiting sequence complementarity or homology to SEQ ID NOS: 1-732 find utility as hybridization probes. In some aspects, the full coding sequence of the transcript, i.e., for SEQ ID NOS: 1-732, are known. Accordingly, any portion of the known sequences available in GenBank, or homologous sequences, can be used in the methods of this invention.

It is known in the art that a "perfectly matched" probe is not needed for a specific hybridization. Minor changes in probe sequence achieved by substitution, deletion or insertion of a small number of bases do not affect the hybridization specificity. In general, as much as 20% base-pair mismatch (when optimally aligned) can be tolerated. Preferably, a probe useful for detecting the aforementioned mRNA is at least about 80% identical to the homologous region of comparable size contained in the previously identified sequences identified by SEQ ID NOS:1-732, which correspond to previously characterized genes or SEQ ID NOS:1-732, which correspond to known ESTs. More preferably, the probe is 85% identical to the corresponding gene sequence after alignment of the homologous region; even more preferably, it exhibits 90% identity.

These probes can be used in radioassays (e.g. Southern and Northern blot analysis) to detect, prognose, diagnose or monitor various pancreatic or colon cells or tissue containing these cells. The probes also can be attached to a solid support or an array such as a chip for use in high throughput screening assays for the detection of expression of the gene corresponding to one or more polynucleotide(s) of this invention. Accordingly, this invention also provides at least one of the transcripts identified as SEQ ID NOS:1-732, or its complement, attached to a solid support for use in high throughput screens.

The total size of fragment, as well as the size of the complementary stretches, will depend on the intended use or application of the particular nucleic acid segment. Smaller fragments will generally find use in hybridization embodiments, wherein the length of the complementary region may be varied,

such as between about 10 and about 100 nucleotides, or even full length according to the complementary sequences one wishes to detect.

5 Nucleotide probes having complementary sequences over stretches greater than 10 nucleotides in length are generally preferred, so as to increase stability and selectivity of the hybrid, and thereby improving the specificity of particular hybrid molecules obtained. More preferably, one can design polynucleotides having gene-complementary stretches of more than 50 nucleotides in length, or even longer where desired. Such fragments may be readily prepared by, for example, directly synthesizing the fragment by
10 chemical means, by application of nucleic acid reproduction technology, such as the PCR technology with two priming oligonucleotides as described in U.S. Pat. No. 4,603,102 or by introducing selected sequences into recombinant vectors for recombinant production. A preferred probe is about 50-75 or more preferably, 50-100, nucleotides in length.

15 The polynucleotides of the present invention can serve as primers for the detection of genes or gene transcripts that are expressed in pancreatic or colon cells. In this context, amplification means any method employing a primer-dependent polymerase capable of replicating a target sequence with reasonable fidelity. Amplification may be carried out by natural or recombinant
20 DNA-polymerases such as T7 DNA polymerase, Klenow fragment of E.coli DNA polymerase, and reverse transcriptase.

A preferred amplification method is PCR. However, PCR conditions used for each reaction are empirically determined. A number of parameters influence the success of a reaction. Among them are annealing temperature
25 and time, extension time, Mg^{2+} ATP concentration, pH, and the relative concentration of primers, templates, and deoxyribonucleotides. After amplification, the resulting DNA fragments can be detected by agarose gel electrophoresis followed by visualization with ethidium bromide staining and ultraviolet illumination.

30 The invention further provides the isolated polynucleotide operatively linked to a promoter of RNA transcription, as well as other regulatory

sequences for replication and/or transient or stable expression of the DNA or RNA. As used herein, the term "operatively linked" means positioned in such a manner that the promoter will direct transcription of RNA off the DNA molecule. Examples of such promoters are SP6, T4 and T7. In certain
5 embodiments, cell-specific promoters are used for cell-specific expression of the inserted polynucleotide. Vectors which contain a promoter or a promoter/enhancer, with termination codons and selectable marker sequences, as well as a cloning site into which an inserted piece of DNA can be operatively linked to that promoter are well known in the art and commercially available.
10 For general methodology and cloning strategies, see Gene Expression Technology (Goeddel ed., Academic Press, Inc. (1991)) and references cited therein and Vectors: Essential Data Series (Gacsa and Ramji, eds., John Wiley & Sons, N.Y. (1994)), which contains maps, functional properties, commercial suppliers and a reference to GenEMBL accession numbers for various suitable
15 vectors. Preferable, these vectors are capable of transcribing RNA in vitro or in vivo.

Fragment of the sequences shown in SEQ ID NOS:1-732 or their respective complements also are encompassed by this invention, preferably at least 10 nucleotides and more preferably having at least 18 nucleotides. Larger
20 polynucleotides, e.g., cDNA or genomic DNA, which hybridize under moderate or stringent conditions to the polynucleotide sequences shown in SEQ ID NOS:1-732, or their respective complements, also are encompassed by this invention.

In one embodiment, these fragments are polynucleotides that encode
25 polypeptides or proteins having diagnostic and therapeutic utilities as described herein as well as probes to identify transcripts of the protein which may or may not be present. These nucleic acid fragments can be prepared, for example, by restriction enzyme digestion of the polynucleotide of SEQ ID NOS:1-732, or their complements, and then labeled with a detectable marker. Alternatively,
30 random fragments can be generated using nick translation of the molecule. For

methodology for the preparation and labeling of such fragments, see Sambrook et al., (1989) supra.

Expression vectors containing these nucleic acids are useful to obtain host vector systems to produce proteins and polypeptides. It is implied that these expression vectors must be replicable in the host organisms either as episomes or as an integral part of the chromosomal DNA. Suitable expression vectors include viral vectors, including adenoviruses, adeno-associated viruses, retroviruses, cosmids, etc. Adenoviral vectors are particularly useful for introducing genes into tissues *in vivo* because of their high levels of expression and efficient transformation of cells both *in vitro* and *in vivo*. When a nucleic acid is inserted into a suitable host cell, e.g., a procaryotic or a eucaryotic cell and the host cell replicates, the protein can be recombinantly produced. Suitable host cells will depend on the vector and can include mammalian cells, animal cells, human cells, simian cells, insect cells, yeast cells, and bacterial cells constructed using well known methods. See Sambrook et al. (1989) supra. In addition to the use of viral vector for insertion of exogenous nucleic acid into cells, the nucleic acid can be inserted into the host cell by methods well known in the art such as transformation for bacterial cells; transfection using calcium phosphate precipitation for mammalian cells; or DEAE-dextran; electroporation; or microinjection. See Sambrook et al. (1989) supra for this methodology. Thus, this invention also provides a host cell, e.g. a mammalian cell, an animal cell (rat or mouse), a human cell, or a procaryotic cell such as a bacterial cell, containing a polynucleotide encoding a protein or polypeptide or antibody.

When the vectors are used for gene therapy *in vivo* or *ex vivo*, a pharmaceutically acceptable vector is preferred, such as a replication-incompetent retroviral or adenoviral vector. Pharmaceutically acceptable vectors containing the nucleic acids of this invention can be further modified for transient or stable expression of the inserted polynucleotide. As used herein, the term "pharmaceutically acceptable vector" includes, but is not limited to, a vector or delivery vehicle having the ability to selectively target

and introduce the nucleic acid into dividing cells. An example of such a vector is a "replication-incompetent" vector defined by its inability to produce viral proteins, precluding spread of the vector in the infected host cell. An example of a replication-incompetent retroviral vector is LNL6 (Miller, A.D. et al. (1989) BioTechniques 7:980-990). The methodology of using replication-incompetent retroviruses for retroviral-mediated gene transfer of gene markers is well established (Correll et al. (1989) PNAS USA 86:8912; Bordignon (1989) PNAS USA 86:8912-52; Culver, K. (1991) PNAS USA 88:3155; and Rill, D.R. (1991) Blood 79(10):2694-700. Clinical investigations have shown that there are few or no adverse effects associated with the viral vectors, see Anderson (1992) Science 256:808-13.

Compositions containing the polynucleotides of this invention, in isolated form or contained within a vector or host cell are further provided herein. When these compositions are to be used pharmaceutically, they are combined with a pharmaceutically acceptable carrier.

This invention further encompasses genes, either genomic or cDNA, which code for a polypeptide or protein in the cell of interest. The genes specifically hybridize under moderate or stringent conditions to a polynucleotide identified by SEQ ID NOS: 1-732 or their respective complements. The process of identification of larger fragment or the full-length coding sequence to which the partial sequence depicted in SEQ ID NOS:1-732 hybridizes preferably involves the use of the methods and reagents provided in this invention, either singularly or in combination.

Five methods are disclosed herein which allows one of skill in the art to isolate the gene or cDNA corresponding to the transcripts of the invention.

RACE-PCR Technique

One method to isolate the gene or cDNA which code for a polypeptide or protein and which corresponds to a transcript of this invention, involves the 5'-RACE-PCR technique. In this technique, the poly-A mRNA that contains the coding sequence of particular interest is first identified by hybridization to

a sequence disclosed herein and then reverse transcribed with a 3'-primer comprising the sequence disclosed herein. The newly synthesized cDNA strand is then tagged with an anchor primer of a known sequence, which preferably contains a convenient cloning restriction site attached at the 5'end. The tagged cDNA is then amplified with the 3'-primer (or a nested primer sharing sequence homology to the internal sequences of the coding region) and the 5'-anchor primer. The amplification may be conducted under conditions of various levels of stringency to optimize the amplification specificity. 5'-RACE-PCR can be readily performed using commercial kits (available from, e.g., BRL Life Technologies Inc, Clotech) according to the manufacturer's instructions.

Identification of known genes or ESTs

In addition, databases exist that reduce the complexity of ESTs by assembling contiguous EST sequences into tentative genes. For example, TIGR has assembled human ESTs into a databe called THC for tentative human consensus sequences. The THC database allows for a more definitive assignment compared to ESTs alone. Software programs exist (give examples) that allow for assembling ESTs into contiguous sequences from any organism.

Isolation of cDNAs from a library by probing with the SAGE transcript or tag

Alternatively, mRNA from a sample preparation was used to construct cDNA library in the ZAP Express vector following the procedure described in Velculescu et al. (1997) Science 270:484. The ZAP Express cDNA synthesis kit (Stratagene) was used accordingly to the manufacturer's protocol. Plates containing 250 to 2000 plaques are hybridized as described in Rupert et al. (1988) Mol. Cell. Bio. 8:3104 to oligonucleotide probes with the same conditions previously described for standard probes exxcept that the hybridization temperature is reduced to room temperature. Washes are performed in 6X standard-saline-citrate 0.1% SDS for 30 minutes at room temperature. The probes are labeled with ³²P-ATP through use of T4 polynucleotide kinase.

Table 2 - Transcripts increased in colon cancer
**Transcripts increased in only colon primary tumors
 compared to normal colon (61 genes)**

NC: Normal Colon

IU: Colon Primary Tumor

CL: Colon Cancer Cell Line

PT: Pancreatic Primary Tumor

PC: Pancreatic Cancer Cell Line

#	Tag Sequence	Tag Number	NC	TU	CL	PT	PC	Accession	Gene Name
1	CATGCACCTAATTGG	H285759	612	755	411	161	333	F15516	H.sapiens mitochondrial EST sequence (1-t-12) from
2	CATGTGATTTCACCT	H933704	452	595	235	80	314	U35430	Human cytochrome c oxidase subunit III (COIII) pse
3	CATGCCCTGTAAATCCC	H388150	433	549	380	443	197	Z70701	H.sapiens mRNA (fetal brain cDNA c2.11).
								X71347	H.sapiens HNF1-C mRNA.
								X71346	H.sapiens HNF1-B mRNA.
4	CATGCACTACTCACC	H291282	293	527	78	14	83	U09500	Human mitochondrial cytochrome b gene, partial cds
5	CATGGTGAACCCCA(G)	H753750	392	517	389	453	194	X66785	H.sapiens mRNA for transacylase (DBT).
								X17648	Human mRNA for granulocyte-macrophage colony-stimu
								U09087	Human thymopoietin beta mRNA, complete cds.
								U09088	Human thymopoietin gamma mRNA, complete cds.
								U20770	Human metastasis suppressor (KAI1) mRNA, complete
								W15552	zb9Jh11.s1 Soares parathyroid tumor Nbl1PA Homo sap
6	CATGGGCTTAGGGA	H687915	37	372	6	29	11	W32091	zc05d03.s1 Soares parathyroid tumor Nbl1PA Homo sap
								R62866	yi11d07.r1 Homo sapiens cDNA clone 138925 5'.
								X89839	H.sapiens mitochondrial DNA for loop attachment se
7	CATGACTTTCCAAA	H130369	32	272	32	23	20	T11535	A1486F Homo sapiens cDNA clone A1486 similar to Mi
8	CATGTGTTGATGCA	H965434	53	271	6	30	5	T11573	IB1870 Homo sapiens cDNA 3'end similar to Human mi
9	CATGAGGGTGTTTC	H175872	26	218	7	20	10	X12544	Human mRNA for HLA class II DR-beta (HLA-DR B).
10	CATGAGGTCAGGAGA(T)	H177315	93	213	113	148	58	S73483	phosphorylase kinase catalytic subunit PHKG2 homol
								X74301	H.sapiens mRNA for MHC class II transactivator.
11	CATGTTGGCCAGGCT	H1025322	124	194	63	111	51	U28687	Human zinc finger containing protein ZNF157 (ZNF15
								U29119	Human leiomyoma LM-196.4 ectopic sequence from HMG
								U56236	Human Fc alpha receptor b mRNA, complete cds.
								W03751	za62h11.r1 Soares fetal liver spleen INFLS Homo sa
12	CATGATCAGGCCCTC	H214616	97	186	17	41	49	W03770	za63f10.r1 Soares fetal liver spleen INFLS Homo sa

[illegible]

36	CATGGTGAAACCCA	H753749	9	31	22	30	4	T93857	ye42f01.s1 Homo sapiens cDNA clone 120409 3' simil
								W03237	za35b09.r1 Soares fetal liver spleen INFLS Homo sa
								W03326	za63g03.r1 Soares fetal liver spleen INFLS Homo sa
37	CATGGAAACTGAACA	H526210	6	26	17	5	3	X54195	Human line-1 element DNA, host sequence flanking 1
								U29607	Human methionine aminopeptidase mRNA, complete cds
								H95100	yw57b10.r1 Homo sapiens cDNA clone 256315 5' simil
38	CATGACTTTTAAAA	H131009	1	22	4	1	0		Human keratinocyte cDNA, clone 067.
39	CATGGACTGCGTGCC	H555450	0	21	7	9	12	D29062	Human keratinocyte cDNA, clone 713.
								D29563	FB3B5 Homo sapiens cDNA clone FB3B5 3' end.
40	CATGTCAGTGTAGT	H863923	4	21	2	2	1	T03196	H.sapiens CpG DNA, clone 164a10, reverse read cpg1
41	CATGAACCTGTGGTT	H7916	2	20	2	2	1	Z57093	H.sapiens CpG island DNA genomic MseI fragment, cl
								Z60184	H.sapiens CpG island DNA genomic MseI fragment, cl
								Z63649	H.sapiens CpG island DNA genomic MseI fragment, cl
								W31349	zb95d06.s1 Soares parathyroid tumor NbHPA Homo sap
42	CATGGGGGGGGGGT	H699051	0	19	0	0	0		zb96h01.s1 Soares parathyroid tumor NbHPA Homo sap
43	CATGTCGCCGTGCC		2	19	1	0	0	W31448	zc40b06.r1 Soares senescent fibroblasts NbHSF Homo
								W47282	H.sapiens fus mRNA.
44	CATGGGGGGTAACTA	H699144	3	19	15	12	5	X71428	TLS=translocated in liposarcoma [human, mRNA, 1824
								S62140	zb96a06.r1 Soares parathyroid tumor NbHPA Homo sap
								W31782	Human parathyroidin mRNA, complete cds.
								M24398	Human defensin 6 (HD-6) gene, complete cds.
45	CATGTCCTGCCCAT	H883029	3	19	14	27	16		Homo sapiens defensin 6 mRNA, complete cds.
46	CATGAAGTGCAAGA	H47683	0	16	0	0	0	U33317	Human mRNA for T cell receptor V beta 14 CDR3, par
47	CATGGGTATTAAACA	H708358	0	16	0	0	0	M98331	A1225F Homo sapiens cDNA clone A1225 similar to Mi
								D32027	Human fetal brain cDNA 5'-end GEN-051G02.
48	CATGGGCTACACCTT	H684312	2	16	0	2	1	T11701	Human mRNA for dipeptidase.
49	CATGAGGGTGTTC	H175870	1	15	0	0	0	D51783	Homo sapiens (clones MDP4, MDP7) microsomal dipept
50	CATGCAAGGACACAC	H272467	0	13	0	2	0	D13138	RDP=renal dipeptidase [human, kidney, Genomic, 357
									Human alpha-1 collagen gene, 3' end with polyA sit
51	CATGIGGAAATGACC	H950498	0	13	0	167	0	M10629	ym17e04.s1 Homo sapiens cDNA clone 47962 3' simila
52	CATGATCCGCGTGCC	H219514	1	13	3	4	1	H11641	yq51a09.s1 Homo sapiens cDNA clone 199288 3' simil
								R95667	
53	CATGTCCTGTACAC	H875282	1	13	0	0	1		
54	CATGATGTAAAAAAT	H241665	0	11	0	12	14	M74090	Human TB2 gene mRNA, 3' end.

[illegible]

Transcripts increased in both colon primary tumors and colon cancer cell lines compared to normal colon (47 genes)

NC: Normal Colon
 TU: Colon Primary Tumor
 CL: Colon Cancer Cell Line
 PT: Pancreatic Primary Tumor
 PC: Pancreatic Cancer Cell Line

#	Tag Sequence	Tag Number	NC	CT	CL	PT	PC	Accession	Gene Name
1	CATGGCAGCCATCCG	H59350	87	180	230	72	138	U14969	Human ribosomal protein L28 mRNA, complete cds.
2	CATGATGGCTGGTAT	H239333	52	153	318	80	294	X17206	Human mRNA for LLRep3.
3	CATGCCCGTCCGGAA	H355689	87	142	246	178	250	X64707	H.sapiens BBC1 mRNA
4	CATGAGGCTACGGAA	H171113	44	117	167	86	147	X56932	H.sapiens mRNA for 23 kD highly basic protein
5	CATGAGCACCTCCAG	H148949	42	116	197	103	190	Z11692	H.sapiens mRNA for elongation factor 2.
6	CATGCTGGGTTAATA	H502724	29	115	160	75	134	M81757	H.sapiens S19 ribosomal protein mRNA, complete cds
7	CATGGGATTGGCCT	H671654	55	108	222	73	185	M17887	Human acidic ribosomal phosphoprotein P2 mRNA, com
8	CATGTACCATCAATA	H807748	46	107	98	64	189	X53778	H.sapiens hng mRNA for uracil DNA glycosylase.
9	CATGTGGGCAAGCC	H959498	51	103	156	45	152	J02642	Human glyceraldehyde 3-phosphate dehydrogenase mRNA
10	CATGAATCCTGTGGA	H55227	30	95	102	48	156	Z11531	H.sapiens mRNA for elongation factor-1-gamma.
11	CATGGGACCACTGAA	H660601	36	92	114	43	63	M55409	Human pancreatic tumor-related protein mRNA, 3' en
12	CATGAGGGCTCCAA	H174037	47	91	167	91	155	Z28407	H.sapiens mRNA for ribosomal protein L8.
13	CATGAAGGTGGAGGA	H44683	48	91	182	113	215	X73460	H.sapiens mRNA for ribosomal protein L3.
14	CATGTGCAGTTTTC	H935680	45	87	105	61	122	M73791	Human novel gene mRNA, complete cds.
15	CATGTCAGATCTTG	H861056	37	81	93	50	92	M64241	Human Wilms' tumor-related protein (QM) mRNA, comp
16	CATGTGTTGTTGAGG	H965603	42	79	83	55	250	M64241	Human Wilms' tumor-related protein (QM) mRNA, comp
17	CATGCCTAGCTGGAT	H379369	28	77	80	46	143	S35960	laminin receptor homolog {3' region} [human, mRNA
18	CATGCTTGGTTTGG	518912	0	73	42	0	0	X80822	H.sapiens mRNA for ORF.
19	CATGCTCCTCACCTG	H482584	12	72	41	34	50	X03342	Human mRNA for ribosomal protein L32
								M58438	Human ribosomal protein S4 (RPS4X) isoform mRNA, c
								M22146	Human scar protein mRNA, complete cds.
								X69150	H.sapiens mRNA for ribosomal protein S18.
								L06432	Homo sapiens 18S ribosomal protein (HKE3) mRNA seq
								Y00052	Human mRNA for T-cell cyclophilin.
								X07868	Human DNA for insulin-like growth factor II (IGF-2);
								U16811	Human Bak mRNA, complete cds.

20	CATGCTGTTGGTGA	H507577	17	65	116	48	103	D14530	Human homolog of yeast ribosomal protein S28, comp
21	CATGCCCGGAACAC	H416261	28	62	183	55	94	X73974	H.sapiens HRPLA mRNA.
22	CATGCAATAAATGTT	H274492	9	60	73	55	119	D23661	Human mRNA for ribosomal protein L37, complete cds
23	CATGACATCATCGAT	H79065	15	57	82	42	118	L06505	Human ribosomal protein L12 mRNA, complete cds.
24	CATGTTCAATAAAAA	H100193	12	56	154	49	99	M17886	Human acidic ribosomal phosphoprotein P1 mRNA, com
25	CATGGAACACATCCA	H528694	24	56	71	24	146	X63527	H.sapiens mRNA for ribosomal protein L19.
26	CATGTTATGGGATCT	H998030	7	55	78	35	77	M24194	Human MHC protein homologous to chicken B complex
27	CATGGCATAATAGGT		18	53	50	19	61	U14967	Human ribosomal protein L21 mRNA, complete cds.
28	CATGAATCTCCAGTA	H253260	23	50	103	49	120	X55954	Human mRNA for HL23 ribosomal protein homologue.
29	CATGACTCCAAAAA	H119809	15	49	64	21	64	X52839	Human mRNA for ribosomal protein L17.
30	CATGCTGTTGATTGC	H507455	9	44	54	22	40	H38868	yp61a04.r1 Homo sapiens cDNA clone 191886 5' simil
31	CATGTACAAAAATCGA	802871	0	42	20	0	0	H71935	ys15f12.r1 Homo sapiens cDNA clone 214895 5'.
32	CATGGAAAAATGGTT	H524524	14	41	81	15	57	Z43914	H.sapiens partial cDNA sequence; clone c-10d03.
33	CATGAAGAAGATAGA	H33331	9	39	69	30	56	T48545	hbc3221 Homo sapiens cDNA clone hbc3221 5'end.
34	CATGCCCTCGAGATC	H390692	12	36	51	25	86	X04347	Human liver mRNA fragment DNA binding protein UP1
35	CATGACTGGGTCTAT	H125661	5	29	25	25	38	X00910	Human mRNA for IGF-II precursor (insulin-like grow
36	CATGACGCTCACTGA	H302367	9	29	40	27	31	X61156	H.sapiens mRNA for laminin-binding protein.
37	CATGGTGTGTTGTA	H769020	0	24	15	22	8	J03799	Human colon carcinoma laminin-binding protein mRNA
38	CATGGTGCCTGAGC	H760291	0	22	17	44	18	U02032	Human ribosomal protein L23a mRNA, partial cds.
39	CATGGTTACATAATAG	H774461	3	22	25	141	10	U14970	Human ribosomal protein S5 mRNA, complete cds.
40	CATGTGAAATAAAAC	H918273	2	18	37	8	22	X38965	H.sapiens RNA for nm23-H2 gene.
41	CATGAAAGAAACTT	H2056	1	16	27	11	25	M36981	Human putative NDP kinase (nm23-H2S) mRNA, complet
42	CATGTGCTGCCTGTT	H948604	1	15	16	11	3	L16785	Human sapiens c-myc transcription factor (pu) mRNA
43	CATGCTGATGGCAGA	H495251	0	14	15	8	6	L10376	Homo sapiens c-myc transcription factor (pu) mRNA
								S80520	Human (clone CTG-B33) mRNA sequence.
								M77349	CAG-isl 7 {trinucleotide repeat-containing sequenc
								X58536	Human transforming growth factor-beta induced gene
								X00497	Human mRNA for HLA class I locus C heavy chain.
								X16934	Human mRNA for HLA-DR antigens associated invarian
								Y00345	Human hb23 gene for B23 nucleophosmin.
								X81005	Human mRNA for polyA binding protein.
								D28137	H.sapiens HCG IV mRNA.
								W46476	Human mRNA for BST-2, complete cds.
								X72718	Soares senescent fibroblasts NbHSF Homo sapiens cDNA clone
									324128 3'.
									H.sapiens DNA for orphan TCR V-beta segment (allele)

44	CATGACTCGCTCTGT	H121311	0	12	16	5	7	H121311	Soares fetal heart NbHH19W Homo sapiens cDNA clone 342926 3'.
								AA305589	EST176663 Colon carcinoma (Caco-2) cell line II Homo sapiens cDNA 5' end
45	CATGGCCCAAGGACC	H610466	0	12	19	82	17	X53416	Human mRNA for actin-binding protein (filamin) (AB
46	CATGATCTTGTTACT	H229106	0	11	28	67	0	X02761	Human mRNA for fibronectin (FN precursor).
47	CATGAAGCTGCTGGA	H40571	0	10	17	6	6	Z26305	H.sapiens isoform 1 gene for L-type calcium channe

Transcripts increased in only colon cancer cell lines compared to normal colon (181 genes)

NC: Normal Colon

TU: Colon Primary Tumor

CL: Colon Cancer Cell Line

PT: Pancreatic Primary Tumor

PC: Pancreatic Cancer Cell Line

#	Tag Sequence	Tag Number	NC	TU	CL	PT	PC	Accession	Gene Name
1	CATGTGTGTTGAGAG	H978825	71	79	487	136	412	X16869	Human mRNA for elongation factor 1-alpha
2	CATGGCCGAGGAAGG	H615043	72	66	265	105	125	X33505	Human ribosomal protein S12.
3	CATGCCAAACCATCCA	H263478	137	83	245	36	502	X12883	Human cyokeratin 18.
4	CATGCACAAACGGTA	H278636	63	53	201	74	179	L19739	Homo sapiens metallopanstimulin (MPSI)
5	CATGAAAAA	H1	31	48	186	66	102	X83412	H.sapiens B1 mRNA for mucin.
								Z32564	H.sapiens FRGAMMA mRNA (819bp) for folate receptor
								X76180	H.sapiens mRNA for lung amiloride sensitive Na+ ch
								U08470	Human FR-gamma' mRNA, complete cds.
								U08471	Human folate receptor 3 mRNA, complete cds.
								S64030	Human L41 ribosomal protein
6	CATGTTGGTCTCTG	H1027448	115	128	179	104	358		ye0202.r1 Homo sapiens cDNA clone 116571 5'.
7	CATGCTCTCCATACCC	H906438	0	0	176	48	0	T91925	H.sapiens ribosomal protein L37a.
8	CATGAAGACAGTGGC	H133979	59	61	172	55	252	X66699	Human ribosomal protein S16
9	CATGCCGTCCAAAGG	H1374027	50	39	138	60	108	M60854	Human thymosin beta 10
10	CATGGGGGAAATCGC	H169375	90	90	136	203	211	M92381	H.sapiens mRNA for ribosomal protein L31.
11	CATGAAGGAGATGGG	H41531	30	37	133	38	161	X69181	Human ribosomal protein L27a
12	CATGGAGGGAGTTTC	H567488	38	53	112	65	142	U14968	H.sapiens ribosomal protein L11.
13	CATGCGCTGGTTCCA	H424694	42	64	111	53	49	X79234	Human ribosomal protein S6
14	CATGGCCGTGTCGCG	H618199	56	39	109	28	120	J03537	Human ribosomal protein S28 mRNA, complete cds
15	CATGGACGACACGAG	H549145	32	59	105	44	70	U58682	Human mRNA for ribosomal protein L17
16	CATGTCACCCACACC	H857362	36	48	103	44	65	X52839	Human ribosomal protein L35
17	CATGCCGCCCGGCT	H416106	39	43	90	52	184	U12465	Human acidic ribosomal phosphoprotein P0
18	CATGCTCAACATCTC	H475448	27	41	89	27	145	M17885	Human M2-type pyruvate kinase mRNA, complete cds.
19	CATGTGGCCCCACCC	H955718	20	30	80	46	55	M23725	Human TCB gene encoding cytosolic thyroid hormone-
								M26252	Human ferritin L chain
20	CATGCCCTGGGTTCT	H359102	34	49	78	92	145	M11147	

21	CATGAGCATCTCCAG	H150997	0	0	77	0	0	H09058	y196f11.r1 Homo sapiens cDNA clone 45943 5'.
								Z44640	H. sapiens partial cDNA sequence; clone c-26605.
								N75111	y229e01.r1 Homo sapiens cDNA clone 284472 5'.
22	CATGGCCTGTATGAG	H621369	24	32	77	33	99	M31520	Human ribosomal protein S24 mRNA.
23	CATGAGCTCTCCCTG	H161624	33	39	76	21	67	X53777	Human L23 mRNA for putative ribosomal protein.
									gb AA223340 AA223340 Homo sapiens cDNA clone 650651 3' similar to
24	CATGCCAGGAGGAAT	H338081	27	12	74	23	87	AA223340	gb:Y00371.mal1 HEAT SHOCK COGNATE 71 KD PROTEIN (HUMAN)
25	CATGGCAAGCCCCA	H672342	30	55	72	27	61	U12404	Human Csa-19
26	CATGAGGAAAGCTGC	H163999	31	42	70	32	146	F16378	H. sapiens EST sequence (135-18) from skeletal muscle
27	CATGAACGCGGCCAA	H26261	29	46	69	54	79	Z23063	Homo sapiens macrophage migration inhibitory factor
28	CATGCCAGAACAGAC	H335945	23	39	66	12	148	X79238	H. sapiens ribosomal protein L30.
29	CATGGCCGCCATCTC	H615736	7	10	65	10	22	U55017	Human transketolase (TKT)
30	CATGGTGTAAACAG	H769045	16	19	65	17	76	L25899	Human ribosomal protein L10
31	CATGCCTCGGAAAT	H383489	9	13	64	23	46	Z26876	H. sapiens ribosomal protein L38.
32	CATGAGGTCTAGCC	H177610	15	27	63	43	41	X06547	Human class Pi glutathione S-transferase
33	CATGGTTCCCTGGCC	H775658	31	26	63	32	96	X65923	H. sapiens fau mRNA.
34	CATGTAAGGAGCTGA	H796831	32	58	62	42	68	X77770	H. sapiens RPS26
35	CATGAACATAAAAAA	H28673	7	14	60	17	39	W52460	ze45e11.r1 Soares senescent fibroblasts NBHSF Homo
								N92893	zb71h03.s1 Homo sapiens cDNA clone 309077 3'.
36	CATGATTTGTCCAG	H260949	17	13	57	9	91	X14957	Human hmg1 mRNA for high mobility group protein I.
37	CATGATAATCTTTG	H200576	13	27	53	30	69	U14973	Human ribosomal protein S29
38	CATGCCCCAGCCAGT	H348756	18	23	53	5	85	U14990	Human XPIPO ribosomal protein S3 (rps3)
39	CATGGGAGTGGACAT	H667269	15	13	49	13	45	L11566	Homo sapiens ribosomal protein L18 (RPL18)
40	CATGTAAAAAATAAA	H786433	13	8	48	10	26	H08238	y187a01.r1 Homo sapiens cDNA clone 44932 5'.
41	CATGGTGTTCACAA	H769605	19	21	48	21	47	X79239	H. sapiens ribosomal protein S13.
42	CATGCCAGGCCAGC	H608595	6	21	47	11	15	U31657	Human unknown protein mRNA, partial cds.
								H41030	yn92a10.r1 Homo sapiens cDNA clone 175866 5'.
43	CATGGGCTCCCACTG	H685384	14	24	47	23	15	M16660	Human 90-kDa heat-shock protein
44	CATGCAACTTCTGG	H853983	0	0	46	2	0	N57419	yw82e04.r1 Homo sapiens cDNA clone 258750 5' simil
45	CATGGATGCTGCCAA	H583573	6	12	46	27	18	X59357	Human mRNA for Epstein-Barr virus small RNAs (EBER)
								L21756	Homo sapiens acute myeloid leukemia associated protein
								D17652	Human mRNA for HBp15/L22, complete cds.
								M64716	Human ribosomal protein S25
46	CATGAATAGGTCCAA	H51925	13	31	46	47	53	M64716	Homo sapiens ribosomal protein S20 (RPS20)
47	CATGGCTTTAAGGA	H655115	8	26	45	22	63	L06498	Human S-adenosylhomocysteine hydrolase (AHCY)
48	CATGAATGCAGCAG	H58533	2	12	44	6	27	M61831	

49	CATGGCCAGCTGGA	H610939	8	18	43	0	22	221507	Human elongation factor 1 delta (EF 1delta)
50	CATGGCCGCTTCG	H678334	6	6	42	8	18	M13932	Human ribosomal protein S17 mRNA
51	CATGTGAGGGAATAA	H928269	14	26	42	15	42	M10036	Human triosephosphate isomerase
52	CATGTGTACCTGTAA	H968173	14	24	42	35	49	K00558	human alpha-tubulin
53	CATGGGCAAGAGAA	H672265	8	7	41	12	87	L19527	Homo sapiens ribosomal protein L27 (RPL27)
54	CATGAACTAACAAA	H28737	6	14	40	14	15	X63237	H.sapiens Uba80 mRNA for ubiquitin.
55	CATGTATACGCTCAG	H837237	0	0	38	0	9		Unknown
56	CATGTACAAGAGGAA	H803369	7	17	38	14	42	X69391	H.sapiens ribosomal protein L6.
57	CATGGTTACGTCCC	H770486	8	17	38	12	25	H11182	ym14a02.r1 Homo sapiens cDNA clone 47866 5'
								T40302	ya31g04.r5 Homo sapiens cDNA clone 62262 5'
								T89480	yd98a05.r1 Homo sapiens cDNA clone 116240 5'
								H01362	yi99c06.r1 Homo sapiens cDNA clone 147370 5'
58	CATGGAGACTCTGC	H558943	13	12	38	32	10	H94371	yw54e05.r1 Homo sapiens cDNA clone 256064 5'
59	CATGATCCACATCGC	H217399	3	10	37	10	14	T49412	ya75b09.r1 Homo sapiens cDNA clone 67481 5'
								T51058	yb55a12.r1 Homo sapiens cDNA clone 75070 5'
								X07270	Human heat shock protein hsp86.
60	CATGGAAGCTTTGCA	H534522	11	13	37	14	25	M91670	Human ubiquitin carrier protein (E2-EPP)
61	CATGCTGGGAGCGC	H501287	2	9	36	3	18	X74070	H.sapiens transcription factor BTF 3.
62	CATGCTGAGACAAAG	H493633	13	8	36	8	26	V00599	Human beta-tubulin
63	CATGAACGACCTCGT	H24951	7	13	35	22	40	X84694	H.sapiens mRNA for elongations factor Tu-mitochondria
64	CATGGCATAGGCTGC	H602783	9	16	35	2	17	L38995	Homo sapiens nuclear-encoded mitochondrial elongation factor
								S75463	P43-mitochondrial elongation factor homolog [human
								H48893	yq80b12.r1 Homo sapiens cDNA clone 202079 5'
65	CATGCATCTTCACCA	H319302	12	14	35	9	16	X71973	H.sapiens GPx-4 mRNA for phospholipid hydroperoxidase
66	CATGGCCTGCTGGC	H621035	10	5	32	18	107	M95787	Human 22kDa smooth muscle protein (SM22)
67	CATGACAGGCTACGG	H76231	0	5	31	64	0	H80294	yu59g01.s1 Homo sapiens cDNA clone 230448 3'
68	CATGGAAATGTAAGA	H528067	5	12	31	14	25	R74294	yi57f06.r1 Homo sapiens cDNA clone 143363 5'
								L36055	Human 4E-binding protein 1
69	CATGGAAGCCAGCCA	H513798	1	3	30	9	11	F17005	H.sapiens EST sequence (011-T1-18) from skeletal muscle
70	CATGTIACCAATATCA	H988366	10	28	30	19	86	H10519	yi90g04.r1 Homo sapiens cDNA clone 45563 5'
71	CATGTTGCTCACAAA	H1023249	1	2	29	1	2		Unknown
72	CATGTCCCGCTCGA	H874103	0	6	29	0	0	X04409	Human coupling protein G(s) alpha-subunit
73	CATGATTACAAAGC	H246019	8	9	29	25	26	X56998	Human Uba52 adrenal mRNA for ubiquitin-52 amino acid
74	CATGCAGATCTTGT	H298495	2	7	28	8	24	F19234	H.sapiens EST sequence (005-X3-16) from skeletal m
75	CATGGTTCGTGCCAA	H777109	9	28	28	17	46	X52317	Human histone H2A.Z.
76	CATGGACGTGTGGC	H552683	3	4	27	2	16		

77	CATGCTAAAAA	H458753	M33680	Human 26-kDa cell surface protein TAPA-1
78	CATGGGGTTTTATT	H704500	L28809	Homo sapiens dbpB-like protein
79	CATGCCGATCACCGG	H363799	M29336	Human translational initiation factor 2 beta subunit
80	CATGGCAAGAAGA	H394051	W07137	za92a11.r1 Soares fetal lung NbHL19W Homo sapiens
			D20503	Human HL60 3'directed Mbol cDNA, HUMGS01477, clone
			N91592	Soares fetal lung NbHL19W Homo sapiens cDNA clone 303055 3'
				yy84c07.s1 Homo sapiens cDNA clone 249420 3' similar to contains Alu repetitive element;
			H83884	
81	CATGTCTCTACCCAC	H908373	Z22572	H.sapiens CDE1 binding protein mRNA.
			L09209	Homo sapiens amyloid protein homologue mRNA, compl
			L19597	Human binding protein mRNA, partial cds.
			S60099	Human binding protein precursor protein homolog [human, pla
82	CATGGTTTCCCAAG	H783697	W07587	APPH=amyloid precursor protein homolog [human, pla
			N28502	zb06f02.r1 Soares fetal lung NbHL19W Homo sapiens
			N35630	yx36f06.r1 Homo sapiens cDNA clone 263843 5'
			Z40265	yx62a03.r1 Homo sapiens cDNA clone 266284 5'
83	CATGCCTGTCCAGCC	H388426	W02723	H. sapiens partial cDNA sequence; clone c-1xe03.
			N24893	zc65c03.s1 Soares fetal heart NbHH19W Homo sapiens
			N32178	yx99h09.s1 Homo sapiens cDNA clone 269921 3'
			H21873	yy25b09.s1 Homo sapiens cDNA clone 272249 3'
84	CATGTCATCATCTGA	H865503	H21873	yl34b10.s1 Homo sapiens cDNA clone 160123 3' simil
			H26394	yl48e12.s1 Homo sapiens cDNA clone 161518 3' simil
			H69857	yr88d02.s1 Homo sapiens cDNA clone 212355 3' simil
			H70714	yu69b11.s1 Homo sapiens cDNA clone 239037 3' simil
			X55110	Human mRNA for neurite outgrowth-promoting protein
85	CATGCCCTGCCCTGT	H358783	X03168	Human mRNA for S-protein.
86	CATGGCCGGGCCCTC	H617048	AA143561	zo32d09.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 588593
87	CATGTTGCTCAAAAA	H1023233	AA152342	3' similar to contains LTR7.1 LTR7 repetitive element
			AA115727	zo01g11.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 566468
				3' similar to contains LTR7.13 LTR7 repetitive element ;
				zl86h11.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 511557
				3' similar to contains LTR7.1 LTR7 repetitive element
88	CATGCAAAATCAGGA	H262987	R76502	yl61f09.r1 Homo sapiens cDNA clone 143753 5'
			T32681	EST52915 Homo sapiens cDNA 5' end similar to None.
			T34662	EST72468 Homo sapiens cDNA 5' end similar to None.
89	CATGGAAGATGTGGG	H533435	H04634	yl49h03.r1 Homo sapiens cDNA clone 152117 5'

									F00364	H. sapiens partial cDNA sequence; clone 76D12; ver yj21c05.s1 Homo sapiens cDNA clone 149384 3'.
90	CATGGTGTCTCATTTCA	H761150	0	8	23	6	4		H01503 H84813 H84956	yv86c02.s1 Homo sapiens cDNA clone 249602 3' simil yv88f07.s1 Homo sapiens cDNA clone 249829 3' simil Homo sapiens putative transmembrane protein (B5)
91	CATGGCTTTACTTTG	H654464	4	5	23	9	5		L38961	Homo sapiens putative transmembrane protein (B5)
92	CATGTTTTCTGA AAAA	H1046401	6	13	23	10	10		J04026	Human thioredoxin (TXN) mRNA
93	CATGTTTGCTCACACA	H1023250	1	4	22	0	4		D11078	Human RGH2 gene.
94	CATGGAATTTCACAGC	H589267	0	0	22	0	19		X53279	Human mRNA for placental-like alkaline phosphatase
95	CATGAGGAGGGAGGC	H166539	2	3	22	2	4		M77836	Human pyrroline 5-carboxylate reductase mRNA,
96	CATGGCTTAACCTGG	H651359	3	4	22	2	4		X07674	Human glutamate dehydrogenase
97	CATGCTCTTCGAGAA	H490889	4	8	22	27	19		Y00433	Human mRNA for glutathione peroxidase
98	CATGAGAACA AAACC	H132098	1	7	21	9	6		X67951	H.sapiens mRNA for proliferation-associated gene
99	CATGCCCGAGGAGAA	H346761	3	3	21	2	24		U38846	Human stimulator of TAR RNA binding (SRB)
									D16933	Human HepQ2 3' region cDNA, clone hmd4fl1.
									U42376	Human retinoic acid induced RIG-E
100	CATGCACTTCAAGGG	H294155	0	3	20	47	107		Unknown	
101	CATGGCGGAGAGAGG	H631331	2	3	20	4	1		Unknown	
102	CATGTTACCTCCCTC	H989024	4	7	20	3	22		F17524	H.sapiens EST sequence (012-T2-32) from skeletal m
103	CA1GAC'TCTGCCAAG	H122449	4	7	20	3	7		Unknown	
104	CA1GTCAGATGGCGT	H861095	1	6	19	12	7		W52942	zc03i05.r1 Soares parathyroid tumor NbHPA Homo sap
105	CATGGGCCCTTTT'T'	H679936	1	3	19	5	3		R21316	yv48t11.l.r1 Homo sapiens cDNA clone 35917 5' sinilia
106	CA1G1GGACGCGCTG	H951912	0	0	19	0	0		X00366	Human lipoprotein apoA.I.
107	CA1GCTGTCTCCCTG	H386904	0	5	19	6	5		M80244	Human E16 mRNA
108	CATGGCCACACCCCA(C)	H607318	2	6	18	18	15		H27927	y158c11.s1 Homo sapiens cDNA clone 162452 3' simil
109	CATGATTATTTTCT	H249854	2	3	18	5	20		X57959	H.sapiens ribosomal protein L7.
110	CATGGAACCTCTGGG	H529899	2	7	18	5	15		AA299898	EST12509 Uterus tumor 1 Homo sapiens cDNA 5' end
111	CATGGGCTGATGTGG	H686319	3	5	18	8	17		U09510	Human glycyl-tRNA synthetase .
112	CATGTC AATAAGAA	H835049	3	10	18	4	4		X76013	H.sapiens QRSHs mRNA for glutaminyl-tRNA synthetas
113	CATGAAAAGTGAAGAT	H11785	0	7	17	0	5		W16529	zb10a1.l.r1 Soares fetal lung NbHL19W Homo sapiens
									W35192	zc70b05.r1 Soares fetal heart NbHH19W Homo sapiens
									W52451	zc45d09.r1 Soares senescent fibroblasts NbHSF Homo
114	CATGCACGCGCTCAA	H288373	0	1	17	0	3		D38251	Human mRNA for RPB5 (XAP4)
115	CATGA ACTAA TACTA	H28872	1	6	17	13	31		D52570	Human fetal brain cDNA 5'-end GEN-081G12.
									D52758	Human fetal brain cDNA 5'-end GEN-087A08.
									D55953	Human fetal brain cDNA 5'-end GEN-407H12.
116	CATGCTGTACCTGGA	H504187	1	0	17	12	6		M22490	Human bone morphogenetic protein-2B (BMP-2B)

117	CATCGGACCCACGCG	H398663	2	6	17	48	0	M12529	Human apolipoprotein E
118	CATGTAGAAAAATAA	H819213	0	1	16	2	7	X16539	H.sapiens RNA for neuroleukin gene.
								M27691	Human transactivator protein (CREB) mRNA, complete
								M86667	Human transactivator protein (CREB) mRNA, complete
119	CATGATCTTGAAGG	H228867	0	0	16	5	3	X33743	H.sapiens NAP (nucleosome assembly protein)
120	CATGCAGCTGGCCAT	H302741	0	1	16	14	0	X33743	H.sapiens mRNA for fibulin-1 C.
121	CATGATCTTGAAGG	H228867	0	0	16	5	3	Z26328	H.sapiens partial cDNA sequence; clone HEC059
121	CATGATCTTGAAGG	H228867	0	0	16	5	3	Z26328	H.sapiens partial cDNA sequence; clone HEC059
121	CATGATCTTGAAGG	H228867	0	0	16	5	3	Z26328	H.sapiens partial cDNA sequence; clone HEC059
122	CATGGTGGAGGTGCG	H762554	2	10	16	3	5	U22035	Human 100 kDa coactivator mRNA
123	CATGGTGGACCCAA	H762197	1	5	15	7	10	R91724	yp98e02.r1 Homo sapiens cDNA clone 193482 5' simil
								W51770	zc48a02.r1 Soares senescent fibroblasts NbHSF Homo
								N42086	yy05b03.r1 Homo sapiens cDNA clone 270317 5'
								R80990	yi94c02.r1 Homo sapiens cDNA clone 146882 5'
124	CATGGAGCAGCTGGA	H561787	0	5	15	2	4	R95036	yy44f01.r1 Homo sapiens cDNA clone 198649 5' simil
								F16507	H.sapiens EST sequence (147-09) from skeletal muscle
125	CATGGCGGGAGGGCT	H633002	1	6	15	8	7	T50201	yb77h05.r1 Homo sapiens cDNA clone 77241 5' simila
								S85655	Human prohibitin
126	CATGATTGGCTTAAA	H256497	1	8	15	0	16	M38188	Human unknown protein from clone pHGR74 mRNA, comp
127	CATGGAAAAATTAA	H524541	0	3	15	4	0	Y00711	Human lactate dehydrogenase B (LDH-B)
128	CATGGATCACAGTTT	H577840	0	5	15	0	0	D83174	Human collagen binding protein 2.
129	CATGAGCCTTTGTTG	H153632	1	2	15	23	5	X70940	H.sapiens elongation factor 1 alpha-2.
130	CATGCTCGACCTCC	H910430	0	0	15	0	2	T30623	EST19638 Homo sapiens cDNA 5' end similar to None.
131	CATGAACAGAAGCAA	H18469	0	2	15	3	11	C01011	HUMGS0004747, Human Gene Signature, 3'-directed cDNA sequence.
								zm62d06.s1	Stratagene fibroblast (#937212) Homo sapiens cDNA clone
								AA111865	530219 3'
								W56516	zd16c08.r1 Soares fetal heart NbHH19W Homo sapiens
								H30299	yo77d04.r1 Homo sapiens cDNA clone 183943 5' simil
132	CATGTGTTCCAGGACC	H980130	1	1	14	5	11	H50265	yo28c02.r1 Homo sapiens cDNA clone 179234 5'
								W01702	za37a06.r1 Soares fetal liver spleen INFLS Homo sa
133	CATGTAGATAATGGC	H822331	1	4	14	6	14	W04495	za38b10.r1 Soares fetal liver spleen INFLS Homo sa
								W23528	zc71g11.s1 Soares fetal heart NbHH19W Homo sapiens
								D11838	Human HepG2 3'-directed Mbol cDNA, clone hm02e09.
134	CATGCTTAATCCTGA	H508767	0	6	14	6	12	X75598	H.sapiens nm23H1 gene.
135	CATGGGCAGAGGACC	H673954	0	6	14	5	11	T35470	EST85850 Homo sapiens cDNA 5' end similar to None.
136	CATGTGACTGAAGCC	H925194	0	5	14	3	0	T35536	EST86951 Homo sapiens cDNA 5' end similar to None.

137	CATGGATAGTTGTGG	H576495	0	1	14	2	1	T35545	EST87066 Homo sapiens cDNA 5' end similar to None.
								H01694	y133g1.1.s1 Homo sapiens cDNA clone 130596 3'.
								N78851	z617d08.s1 Homo sapiens cDNA clone 302319 3'.
								N78931	za92h06.s1 Homo sapiens cDNA clone 300059 3'.
138	CATGGTGGTGGACAC	H765573	1	4	13	6	13	H90469	yv01e06.r1 Homo sapiens cDNA clone 241474 5' simil
								R76765	y163g01.r1 Homo sapiens cDNA clone 143952 5' simil
								T35045	EST79335 Homo sapiens cDNA similar to None...
139	CATGTGGGGTACCTT	H961304	0	6	13	2	9	H51447	yo31a05.r1 Homo sapiens cDNA clone 179504 5'.
								W46469	zc32c05.r1 Soares senescent fibroblasts NBHSF Homo
								W51800	zc48e04.r1 Soares senescent fibroblasts NBHSF Homo
								R33196	yh77f08.r1 Homo sapiens cDNA clone 135783 5'.
								J04799	Human prothymosin-alpha
140	CATGTTTCATTATAAT	H1003313	1	10	13	8	10	D80012	Human KIAA0190 protein
141	CATGCTTCTGTGTAC(T)	H515821	0	5	13	8	12	U02389	Human hLON ATP-dependent protease mRNA
142	CATGACTGGCGAAGT	H125315	1	5	13	2	5	T29819	EST96617 Homo sapiens cDNA 5' end similar to ATP-d
								X14850	Human histone H2A.X.
143	CATGGAAGAGCTGA	H526495	1	3	13	1	6	J04088	Human DNA topoisomerase II (top2) mRNA
144	CATGCAACTCTATGG	H269775	0	1	13	1	2	K01891	Human beta globin retrovirus-like repetitive element
145	CATGAAATTGGTGC	H16303	0	0	13	0	0	I188396	EST28e05 Homo sapiens cDNA clone 28e05
								X74796	H. sapiens p85Mcm mRNA.
146	CATGCTGCACCTTACT	H496114	1	2	13	1	8	D28480	Human mRNA for hMCM2, complete cds.
								D55716	Human B lymphoma mRNA for Plcdc47, complete cds.
147	CATGAATATTGAGAA	H53129	0	5	13	6	11	T30327	EST14849 Homo sapiens cDNA 5' end similar to None.
								T34394	EST66942 Homo sapiens cDNA 5' end similar to None.
								T47475	yb14c03.r1 Homo sapiens cDNA clone 71140 5'.
								T50289	yb14h08.r1 Homo sapiens cDNA clone 71199 5'.
								Unknown	Unknown
148	CATGTCGCCGGCGC	H890535	0	1	13	2	1	H59914	Unknown
149	CATGGGGGCGCCG	H697495	0	2	13	2	7	U33818	Human inducible poly(A)-binding protein
150	CATGCCAAGAAAGAA	H329737	0	6	12	4	4	D16891	Human HepG2 3' region cDNA, clone hmd2c1 l.
151	CATGTTTTTGATAAA	H1048113	0	5	12	4	12	M29882	Human apolipoprotein A-II
152	CATGTGTGGAGAGCC	H977034	0	0	12	0	0	Z49216	H. sapiens mitoxantrone-resistance associated mRNA.
153	CATGCCACGGTTAG	H345789	0	5	12	5	4	Unknown	Unknown
154	CATGAATTCTCCTAA	H63325	0	1	12	1	1	Unknown	Unknown
155	CATGGACCTCCGGGC	H548203	0	0	12	0	0	M93651	Human set gene
156	CATGTGAATCTGGGT	H921067	0	2	11	7	8		

157	CATGTCCTTCTCCAC	H884181	0	5	11	14	8	X13804	Human alpha-actinin.
158	CATGTATCTGTCTAC	H843485	0	4	11	2	3	T19569	609F Homo sapiens cDNA clone 609 similar to SET protein
159	CATGACGTTCTCTTC	H114144	0	0	11	1	17	Z36249	HHEA18W.H. sapiens partial cDNA sequence; clone HEA18W;
									zq73e07.r1 Stratagene neuroepithelium (#937231) Homo sapiens cDNA
160	CATGCCCTGAGTCAG	H358581	0	0	11	0	0	AA207189	clone 647268 5' similar to TR:E16910 E16910 ENDONUCLEASE.;
161	CATGGAAATTCCTCGA	H540023	0	3	11	3	1	N80776	za98h04.s1 Homo sapiens cDNA clone 300631 3'.
									ze90d01.s1 Soares fetal heart NBHH19W Homo sapiens cDNA clone
								AA025809	366241 3'
									zs85h05.s1 Soares NBHTGBC Homo sapiens cDNA clone
								AA279492	3'
162	CATGGACGCCGAAC	H550274	0	1	11	6	0		Unknown
									zk84f04.s1 Soares pregnant uterus NBHPU Homo sapiens cDNA clone
163	CATGGCGGACTGGGG	H631275	0	0	11	1	0	AA098867	489535 3' similar to SW:A5_XENLA P28824 A5 PROTEIN PRECURSOR
164	CATGGGAACACACAG	H656453	0	1	11	0	2	R48460	yj67c12.r1 Homo sapiens cDNA clone 153814 5'.
									zp01c02.r1 Stratagene ovarian cancer (#937219) Homo sapiens cDNA
								AA173819	clone 595106 5'
165	CATGTTGCGGAGCCC	H1022502	0	2	11	2	1	L19183	HUMMAC30X Human MAC30 mRNA, 3' end.
								H61710	yr24a07.s1 Homo sapiens cDNA clone 206196 3'.
								H77330	yu11f12.s1 Homo sapiens cDNA clone 233519 3'.
								N69482	za18d05.s1 Homo sapiens cDNA clone 292905 3'.
166	CATGGCAGACATTGA	H598335	0	7	10	4	9	H41078	yp52c11.s1 Homo sapiens cDNA clone 191060 3' simil
167	CATGCACTGAAAA	H294401	0	1	10	5	0	H04630	yj49g03.r1 Homo sapiens cDNA clone 152116 5'.
168	CATGGGTTGCAGG	H719435	0	0	10	24	0	R77027	yi66e12.r1 Homo sapiens cDNA clone 14238 5'.
169	CATGTTCTCTCGGC	H1007018	0	1	10	4	12	R32331	yh68g02.s1 Homo sapiens cDNA clone 134930 3' simil
170	CATGCTGCCGAGCT	-497192	0	8	10	1	10	T86566	yd77g07.r1 Homo sapiens cDNA clone 114300 5' simil
171	CATGGTGAAAAAA	H753665	0	2	10	3	7	S77357	transcript ch11 [human, RFLP48 stomach cancer c
172	CATGCTGTGCAGCA	H506149	0	6	10	6	1	M34338	Human spermidine synthase
173	CATGATGTTGTGG	-835515	0	1	10	0	2	U03911	Human mutator gene (hMSH2)
174	CATGATGTAGTAGTG	H242380	0	5	10	9	7	D55671	Human heterogeneous nuclear ribonucleoprotein
175	CATGGACCCACTACC	H545906	0	1	10	3	1	J03569	Human lymphocyte activation antigen 4F2 large subunit
176	CATGAAATAGTTTT	H12992	0	1	10	6	3	D53402	Human fetal brain cDNA 5'-end GEN-108D03.
								T61971	yb96f02.r1 Homo sapiens cDNA clone 79035 5'.
								D61243	Human fetal brain cDNA 5'-end GEN-171G06.
								N7240	yy44d02.r1 Homo sapiens cDNA clone 245571 5'.
177	CATGCCCGCGCTGGT	H371131	0	0	10	1	2	T35761	EST90898 Homo sapiens cDNA 5' end similar to EST c

178	CATGGACTGAGCTTG	H555168	0	8	10	3	3	T31901	EST40719 Homo sapiens cDNA 5' end similar to None.
179	CATGAAACGCCCAAT	H6481	0	2	10	1	3	X98264	JHSMPP41 H.sapiens mRNA for M-phase phosphoprotein, mpp4, 1523bp
180	CATGATGAGGCCGGG	H232027	0	4	10	7	1		Unknown
181	CATGGCCCACTCCG(A)	H610614	0	9	10	6	2	D87433	Human mRNA for KIAA0246 gene, partial cds

Table 3 - Transcripts decreased in colon cancer
**Transcripts decreased in only colon primary tumors
 compared to normal colon (51 genes)**

NC: Normal Colon
 TU: Colon Primary Tumor
 CL: Colon Cancer Cell Line
 PT: Pancreatic Primary Tumor
 PC: Pancreatic Cancer Cell Line

#	Tag sequence	Tag Number	NC	CT	CL	PT	PC	Accession	Gene Name
1	CATGGCTTTATTGT	H654591	184	110	185	203	111	X00351	Human mRNA for beta-actin.
2	CATGCTAGCCTCAGG	H468434	170	61	130	80	75	X04098	Human mRNA for cytoskeletal gamma-actin.
3	CATGCAAAACCATCCA	H263478	137	83	245	36	502	X12883	Human mRNA for cytokeratin 18.
4	CATGCTTCCAGCTAA	H513181	64	23	36	53	104	D00017	Human lipocortin II mRNA.
5	CATGCCCCAGTTGCT	H348922	61	27	38	37	46	X04106	Human mRNA for calcium dependent protease (small subunit)
6	CATGGATGACCCCCC	H581974	53	4	42	6	32	Z65313	H.sapiens CpG island DNA genomic Mse I fragment, cl
7	CATGCTGTACAGACA	H504098	50	22	26	6	32	W61077	z30d02.r1 Soares fetal heart NbHH19W Homo sapiens
8	CATGCGGACTCACTG	H427848	47	15	26	18	4	D60944	Human fetal brain cDNA 5'-end GEN-141D02.
9	CATGCCCGCCGGAA	H349801	47	10	21	15	8		Unknown
10	CATGCCGTGAAGAGG	H387107	46	19	39	47	14	J02783	Human thyroid hormone binding protein (p55) mRNA.
11	CATGGCCTGGCCATC	H621140	46	19	24	16	20	N33042	yy05d05.s1 Homo sapiens cDNA clone 270345 3'
12	CATGAGCAGGAGCAG	H150053	43	12	26	24	20	W07627	zb06a05.r1 Soares fetal lung NbHL19W Homo sapiens
13	CATGAACGTGCAGGG	H28235	42	6	57	2	10	X01630	Human mRNA for argininosuccinate synthetase.
14	CATGGCCGCCCTGCA	H615802	40	12	16	17	8	D43682	Human mRNA for very-long-chain acyl-CoA dehydrogen
15	CATGTGGGGAGAGGA	H960651	40	5	36	10	5	D29146	Human keratinocyte cDNA, clone 173.
16	CATGGCTGGCCCTTGA	H648575	38	10	20	6	39	K00557	human alpha-tubulin mRNA, 3' end.
17	CATGTGGCCATCTGC	H955615	37	5	15	19	18	AA341633	AA341633 EST47188 Fetal kidney II Homo sapiens cDNA 5' end
18	CATGCGTCTCTCGG	H456167	35	4	36	8	0	X77956	H.sapiens ldl mRNA.
19	CATGTGCATCTGGTG	H937452	33	9	14	13	10	X87949	H.sapiens mRNA for BIP protein.
20	CATGGTGACCTCCTT	H755160	33	7	12	6	31	J04823	Human cytochrome c oxidase subunit VIII (COX8) mRNA
21	CATGTAGCTCTATGG	H826831	33	5	18	9	13	U16798	Human Na,K-ATPase alpha-1 subunit mRNA, complete c
22	CATGTGCGGTAGGG	H760267	29	7	26	19	27	R50350	gbIR50350R50350 yj59c04.s1 Homo sapiens cDNA clone 153030 3'
								R50013	yj59c04.r1 Homo sapiens cDNA clone 153030 5'.
								C02981	Human Heart cDNA, clone 3NH0642.

23	CATGGGGCGCTGTGG	H694767	28	6	20	6	26	T31329	EST30445 Homo sapiens cDNA 5' end similar to ubiquinol cytochrome-c reductase, 6.4 kDa.
24	CATGCCTCCAGTAC	H382130	27	6	12	3	19		Unknown
25	CATGCCCTGTACAGC	H388627	27	3	14	8	7	H63643	yr34d11.1 Homo sapiens cDNA clone 207189 5' simil
26	CATGTCACAGTGCCT	H856806	24	5	8	17	11	W60924	zd27c08.1 Soares fetal heart NbHH19W Homo sapiens
27	CATGAATAAAGGCTA	H49320	23	5	7	11	13	L25081	Human GTPase (rhoC) mRNA, complete cds.
28	CATGTTGTGTGTGAA	H1031929	23	5	13	15	25	D45887	Human mRNA for calmodulin, complete cds.
29	CATGAAGGTAGCAGA	H44179	23	4	10	16	12	N62815	yy66b11.s1 Homo sapiens cDNA clone 278493 3'.
30	CATGGTGTGGGGGT	H769707	21	2	5	14	10	R68653	yl14b06.s1 Homo sapiens cDNA clone 139187 3'.
31	CATGTGCAGCGCTG	H936344	21	1	5	7	13	X90858	H.sapiens mRNA for uridine phosphorylase.
32	CATGATGGCACGGAG	H238697	20	2	4	0	3	H19458	yn54c02.s1 Homo sapiens cDNA clone 172226 3' simil
33	CATGGCCAGACACC	H608326	20	1	6	1	9	T30468	EST17149 Homo sapiens cDNA 5' end similar to None.
34	CATGCTTCTTGCCCC	H515990	20	0	17	3	0	V00491	Human gene for alpha I globin.
35	CATGACCCACGTCAG	H86453	19	2	7	22	9	X51345	Human jun-B mRNA for JUN-B protein.
36	CATGGGCTGCCTGCC	H686458	18	3	4	5	8	R72429	yl90e08.s1 Homo sapiens cDNA clone 156038 3'.
								R484491	yl67b10.s1 Homo sapiens cDNA clone 153787 3'.
								R52128	yl72b03.s1 Homo sapiens cDNA clone 154253 3'.
								X12910	Human Na ⁺ , K ⁺ A TPase gene exons 1 - 3 (alpha III is
37	CATGGAGGGCCGGTG	H567660	18	2	14	6	16	X12910	Unknown
38	CATGGATGAATCCGG	H581847	17	1	3	2	2		Unknown
39	CATGAGCCCGACCCAC	H153109	16	2	11	7	5	X81006	H.sapiens HCG I mRNA.
40	CATGGTTACGCTGTC	H774780	16	2	12	3	12	L08666	Homo sapiens porin (por) mRNA, complete cds and tr
41	CATGCCTCGCTCAGT	H383443	16	1	8	6	7	U04627	Human 78 kDa gastrin-binding protein mRNA, complet
42	CATGCAATAAAAGT	H265219	15	1	8	9	0	U17077	Human BENE mRNA, partial cds.
43	CATGTGCCGCCCGCA	H940378	15	1	8	0	3	U28369	Human semaphorin V mRNA, complete cds.
44	CATGGCAGTGGCCTC	H601752	15	0	6	4	3	D12038	Human HepG2 3'-directed Mbol cDNA, clone s150.
45	CATGCTGGGCCTGAA	H502137	14	0	3	3	18	U77396	Human TNF-alpha inducible responsive element mRNA,
46	CATGGCCCATTTGGAG	H611305	13	1	6	13	17	Z29093	H.sapiens EDDR1 gene for receptor tyrosine kinase.
47	CATGAAGAAACCTC	H32792	12	0	2	2	0	T94990	yc38a04.s1 Homo sapiens cDNA clone 119982 3'.
								N69310	za25g05.s1 Homo sapiens cDNA clone 293624 3'.
									zb86e03.s1 Soares senescent fibroblasts NbHSF Homo sapiens cDNA
								N98502	clone 310492 3'.
48	CATGGAATGATTCT	H538878	12	0	6	6	14	F18838	H.sapiens EST sequence (007-X1-01) from skeletal m
49	CATGGCCTGGTCCTT	H621272	12	0	3	3	8	AA226928	zz21b10.s1 Striatagene NT2 neuronal precursor 937230 Homo sapiens
50	CCATGGCCACACAG	H610579	11	0	1	1	0	M60047	cDNA clone 664027 3'.
									Human heparin binding protein (HBp17) mRNA

51	CATGGGATTCCAGTT	H671052	11	0	4	3	2	W52456	zc45e09.r1 Soares senescent fibroblasts NbHSF Homo
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Transcripts decreased in both colon primary tumors and colon cancer cell lines compared to normal colon (130 genes)

NC: Normal Colon

TU: Colon Primary Tumor

CL: Colon Cancer Cell Line

PT: Pancreatic Primary Tumor

PC: Pancreatic Cancer Cell Line

#	Tag Sequence	Tag Number	NC	TU	CL	PT	PC	Accession	Gene Name
1	CATGCCCTCCAGCTAC	H182109	803	191	304	136	663	X12882	Human mRNA for cytokeratin 8.
2	CATGCTAAGACTTCA	H460926	708	282	402	142	497	F15636	H.sapiens mitochondrial EST sequence (002T115)
3	CATGGCCCCAGGTAC	H610997	705	58	2	2	1		Unknown
4	CATGACCCCTTGGCCA	H90022	512	348	93	43	235	F16940	H.sapiens mitochondrial EST sequence (009-T1-21) f
5	CATGACATTGGGTGA	H81583	504	92	4	0	0	M10050	Human liver fatty acid binding protein (FABP) mRNA
6	CATGGCGAAACCCCTG	H622680	486	108	27	30	13	S61953	c-erbB3=receptor tyrosine kinase {alternatively sp
7	CATGAGCCCTACAAA	H153361	367	242	132	71	204	F15506	H.sapiens mitochondrial EST sequence (1-t-02) from
8	CATGGACCCCAAGATA	H543828	276	131	0	7	0	T39321	ya04c01.r2 Homo sapiens cDNA clone 60480 5'.
								H24673	y141a01.s1 Homo sapiens cDNA clone 160776 3'.
									HUMGS02706 Human colon 3'directed Mbol cDNA, HUMGS02706, clone cm 1673.
								D25586	
								T96160	ye09b02.s1 Homo sapiens cDNA clone 117195 3'.
9	CATGGCCGGGTGGGC	H617195	256	88	148	144	178	X64364	H.sapiens mRNA for M6 antigen.
10	CATGTTGGGGTTTCC	H1026814	202	75	84	235	369	M11146	Human ferritin H chain mRNA, complete cds.
11	CATGCTCCACCCGAA (or G)	H479577	201	120	0	11	3	L15203	Human secretory protein (P1.B) mRNA, complete cds.
12	CATGGCAGGGCCTCA	H600670	196	68	6	32	19	X93036	H.sapiens mRNA for MAT9 protein.
									yv07h09.r1 Homo sapiens cDNA clone 242081 5' similar to SP-A39484
13	CATGATCGTGGCGGG	H224923	194	24	97	40	39	H93844	A39484 ANDROGEN-WITHDRAWAL APOPTOSIS PROTEIN RVP1.
14	CATGCAAGCATCCCC	H271574	190	99	101	30	139	F17001	H.sapiens mitochondrial EST sequence (011-T1-13) f
15	CATGGACATCAAGTC	H544012	189	33	76	57	219	Y00503	Human mRNA for keratin 19.
									zb05a11.r1 Soares fetal lung NbHL19W Homo sapiens cDNA clone
									301148 5' similar to gb: V00567 BETA-2-MICROGLOBULIN
									PRECURSOR (HUMAN):
16	CATGGTTGTGGTTAA	H782013	178	110	14	340	139	W16632	zo31h04.s1 Stratagene colon (#937204) Homo sapiens cDNA clone
								AA143804	588335 3'

BNSDOCID: <WO 9853319A2.1>

[illegible]

[illegible]

									AA303091	EST12940 Uterus tumor 1 Homo sapiens cDNA 3' end za52d02.r1 Soares fetal liver spleen INFLS Homo sapiens cDNA clone 296163 5'.
63	CATGGCAGCTCCTGT	H599903	43	8	17	24	13		W02429	yx44c11.s1 Homo sapiens cDNA clone 264596 3'.
									N20325	yz13c12.s1 Homo sapiens cDNA clone 282934 3'.
									N45127	zb38c11.s1 Soares parathyroid tumor NbHPA Homo sapiens cDNA clone 305876 3'.
									N90407	Human wild-type p53 activated fragment-1 (WAF1) mR
64	CATGTGTCCTGGTTC	H972720	43	12	14	25	5		U03106	zc11f01.s1 Soares parathyroid tumor NbHPA Homo sapiens cDNA clone 322009 3'.
65	CATGACAAACCCCA	H65878	42	16	7	12	11		W37827	gb W15332 W15332.zc16d10.s1 Soares parathyroid tumor NbHPA Homo sapiens cDNA clone 322483 3'.
									W15332	zc04g10.s1 Soares parathyroid tumor NbHPA Homo sapiens cDNA clone 321378 3'.
									W32410	Human sodium/potassium-transporting ATPase beta-3
									N32312	Unknown
									U51478	Unknown
66	CATGTAGGATGGGG	H828331	41	6	11	6	9			zp44f11.s1 Stratagene muscle 937209 Homo sapiens cDNA clone 612333 3' similar to contains Alu repetitive element;
67	CATGACTGTGGCGC	H126619	41	7	1	4	35			yh87e04.s1 Homo sapiens cDNA clone 136734 3' similar to contains Alu repetitive element.
68	CATGGTAGCAGGTGT	H730287	40	7	13	17	24		AA180815	yh87e04.s1 Homo sapiens cDNA clone 136734 3' similar to contains Alu repetitive element.
									R34696	repetitive element.
									R34696	repetitive element.
									AA194497	zq06e03.s1 Stratagene muscle 937209 Homo sapiens cDNA clone 628924 3' similar to contains Alu repetitive element
										hbc760 Homo sapiens cDNA clone hbc760 3'end similar to nonspecific crossreacting antigen.
69	CATGAATCACAATA	H53508	40	12	0	3	0		T11144	zl67e01.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 509688 3' similar to TR:G189087
									AA058357	similar to none
									C05803	zo31e02.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 588506 3'
									AA143765	zp45b09.s1 Stratagene HeLa cell s3 937216 Homo sapiens cDNA clone 612377 3'
70	CATGAGGATGGTCCC	H167606	40	11	4	4	5		AA179299	

71	CATGCCAAAGCTATA	H328308	38	11	6	2	18	M35252	Human CO-029.
72	CATGCGGAGTCGGG	H434907	38	8	6	0	0	R87448	ym89c10.s1 Homo sapiens cDNA clone 166098 3'.
73	CATGCCCGTGGAGAG	H618121	38	9	5	17	26	X79882	H.sapiens lrp mRNA.
74	CATGCCCCCGAAGCC	H349706	37	6	0	0	0	Unknown	Unknown
75	CATGATTCAAGATG	H259108	37	1	0	0	0	J03037	Human carbonic anhydrase II mRNA, complete cds.
76	CATGCCCCAGTGGCT	H611050	37	3	0	2	10	Unknown	Unknown
77	CATGATGGTGGGGA	H241323	36	2	6	25	2	M92843	H.sapiens zinc finger transcriptional regulator mRNA
78	CATGCCTGCCGCCCT	H386390	35	12	7	7	5	X60188	Human ERK1 mRNA for protein serine/threonine kinase
79	CTAGTGGAAAGTGAA	H950457	34	1	1	12	0	V01512	Human cellular oncogene c-fos (complete sequence).
80	CATGGTCATCACAC	H740629	34	0	0	0	0	U34279	Human uroguanylin mRNA, complete cds.
81	CATGCTTATGTTCCC	H511670	34	1	0	3	1	AA287021	zs57c03.s1 Soares NbHTGBC Homo sapiens cDNA clone 701572 3'.
82	CATGCTGGGCCCTCTG	H502136	34	3	4	11	5	T55226	yb47a01.s1 Homo sapiens cDNA clone 74280 3' containing LI repetitive element
								R37446	yf56e10.s1 Homo sapiens cDNA clone 26129 3' similar to gb:X07173 INTER-ALPHA-TRYPsin INHIBITOR COMPLEX COMPONENT II
								AA406180	zu65c08.s1 Soares testis NHT Homo sapiens cDNA clone 742862 3'.
83	CATGGCCCAAGGGCCC	H610982	33	3	0	0	2	R09752	Unknown
84	CATGTTTACTGAT	H1047673	33	7	0	4	2	R81530	yj02b10.r1 Homo sapiens cDNA clone 147547 5'.
								T32348	EST47211 Homo sapiens cDNA 3' end similar to None..
								W57810	zd17g02.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 340946 3'.
								AA398527	z47e12.s1 Soares ovary tumor NbHOT Homo sapiens cDNA clone 725518 3'.
85	CATGCCTGCTTGTCG	H387054	32	2	1	6	32	X63187	H.sapiens HE4 mRNA for extracellular proteinase inhibitor homologue
86	CATGACCTGGGGAGG	H96931	32	6	4	8	6	Unknown	Unknown
87	CATGCCTTCAAATCA	H390158	31	1	0	0	0	R46266	yg52g07.s1 Homo sapiens cDNA clone 36232 3' similar to gb:M33987 CARBONIC ANHYDRASE I
88	CATGTCGGAGCTGTT	H893564	30	1	4	7	1	H98618	yx12a06.s1 Homo sapiens cDNA clone 261490 3'.
								AA171705	zo97h01.s1 Stratagene ovarian cancer (#937219) Homo sapiens cDNA clone 594865 3'.
								H99212	yx15g08.s1 Homo sapiens cDNA clone 261854 3'.

[illegible]

99	CATGTACCTCTGATT	H810468	27	5	7	11	12	X65614	H.sapiens mRNA for calcium-binding protein S100P.
100	CATGATGATGGCACC	H233106	26	0	2	0	2		
101	CATGTTCTGTAGCCC	H1014566	25	5	0	4	0		embJ26988 HSSERCA3M H.sapiens mRNA for adenosine triphosphatase, calcium
102	CATGCCTGTCTGCCA	H388382	24	1	2	1	3	T99568	ye65c02.r1 Homo sapiens cDNA clone 122594 5'.
								T87539	yd89f09.s1 Homo sapiens cDNA clone 115433 3'.
									gb AA347726 AA347726 EST54132 Fetal heart II Homo sapiens cDNA 5' end similar to transmembrane secretory component
103	CATGTATGATGAGCA	H844682	23	4	0	1	0		
104	CATGCTGGCAAAGGT	H500747	23	0	0	0	0		
105	CATGCTTGATTGCCA	H517078	23	4	4	17	7	L42379	Homo sapiens bone-derived growth factor (BPGF-1) m
106	CATGCTTGACATACC	H516402	22	0	0	7	2	X68277	H.sapiens CL 100 mRNA for protein tyrosine phosphatase hydrolase
107	CATGGCTGGCACATT	H649492	22	5	0	0	0	M82962	Human N-benzoyl-L-tyrosyl-p-amino-benzoic acid alpha subunit (PPH alpha) mRNA, complete cds
108	CATGTCTGAATTATG	H909556	21	1	1	1	1	X16354	Human mRNA for transmembrane carcinoembryonic antigen (CEA)
109	CATGGGAAGAGCACT	H657554	21	1	1	3	3	X74570	H.sapiens mRNA for Gal-beta(1-3/1-4)GlcNAc alpha-2,3-sialyltransferase
110	CATGGCTCTTCCCA	H646998	20	2	0	1	0	R87768	yo45d01.s1 Homo sapiens cDNA clone 180865 3' similar to contains PTRS repetitive element
								R85880	yo36g07.s1 Homo sapiens cDNA clone 180060 3' similar to contains PTRS repetitive element
111	CATGAAATCTGGCAC	H114245	20	2	0	4	3	L20826	Human I-plastin mRNA, complete cds.
112	CATGTAAATTGCAAT	H802708	19	2	0	1	7	Z50751	HSB4BMR H.sapiens mRNA for B4B
								U77085	Human epithelial membrane protein (CL-20) mRNA, complete cds
								Y07909	HSPAPR H.sapiens mRNA for Progression Associated Protein
113	CATGGTGGGGCGCC	H764570	18	1	1	8	2	R48529	yj64g10.r1 Homo sapiens cDNA clone 153570 5'.
									EST10a24 Clontech adult human fat cell library HL1108A Homo sapiens cDNA clone 10a24.
114	CATGTTATGGTGTGA	H998127	17	0	0	1	0	T27534	sapiens cDNA clone 10a24.
115	CATGGGAGAAACAGC	H663571	17	1	2	4	0	T86124	yd84b04.s1 Homo sapiens cDNA clone 114895 3'.
								AA131008	zo15g05.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 587000 3'.
								R49945	yj58g11.s1 Homo sapiens cDNA clone 152996 3'.
								T57044	ya84h01.s1 Homo sapiens cDNA clone 68401 3'.
116	CATGCCAACACCAGC	H328787	17	1	0	0	0		
117	CATGAGGTGACTGGG	H178299	17	0	0	0	0		
118	CATGGCCATCCTCCA	H609654	16	0	0	0	0		gb R73013 R73013 yj94a09.r1 Homo sapiens cDNA clone 156376 5'.

119	CATGTTTCTCGTCGC	H1039799	15	1	0	4	4	M69013	Human guanine nucleotide-binding regulatory protein
120	CATGTCAGAGCGCTG	H860776	15	1	1	1	0	Unknown	Unknown
									yv72h06.s1 Soares fetal liver spleen INFLS Homo sapiens cDNA clone 248315 3' similar to contains element PTR7 repetitive element
121	CATGTTCCGCGTTCC	H1006014	14	1	0	0	2	N58523	Unknown
122	CATGTACGGTGTGGG	H814011	14	1	0	0	0		Unknown
123	CATGCTCAGAACTTG	H477216	14	0	1	4	13		Unknown
124	CATGGGACTAAATGA	H662543	13	1	0	1	0	M29540	Human carcinoembryonic antigen mRNA (CEA), complete cds.
									HUMGS04154 Human colon 3'directed Mbol cDNA, HUMGS04154, clone cm0215.
125	CATGGCTTGGGGATT	H653988	12	0	0	0	1	D25786	yc36e02.r1 Homo sapiens cDNA clone 82778 5' similar to gb:L07765 LIVER CARBOXYLESTERASE PRECURSOR
								T73613	Unknown
126	CATGACCCCAACTGCC	H86138	12	0	0	0	1		Unknown
127	CATGCTGAACCTCCC	H491894	12	0	0	2	2		gb T95615 T95615.ye40e03.s1 Homo sapiens cDNA clone 120220 3'.
									zr19b11.s1 Stratagene NT2 neuronal precursor 937230 Homo sapiens cDNA clone 663837 3'
128	CATGCAAGAGTTTCT	H271102	11	0	0	2	0	AA226797	zq97h01.s1 Stratagene NT2 neuronal precursor 937230 Homo sapiens cDNA clone 649969 3'
								AA218730	yp57f10.r1 Homo sapiens cDNA clone 191563 5' similar to gb:M90657 TUMOR-ASSOCIATED ANTIGEN L6 (HUMAN);.
129	CATGGTCCGAGTGCA	H743610	11	0	0	8	5	H38178	Unknown
130	CATGTTTGGTTTCAC	H1043445	11	0	0	0	0		Unknown

Transcripts decreased in only colon cancer cell lines compared to normal colon (78 genes)

NC: Normal Colon
 TU: Colon Primary Tumor
 CL: Colon Cancer Cell Line
 PT: Pancreatic Primary Tumor
 PC: Pancreatic Cancer Cell Line

#	Tag sequence	Tag Number	NC	TU	CL	PT	PC	Accession	Gene Name
1	CATGCACCTAATTGG	H285759	612	755	411	161	333	F15516	H.sapiens mitochondrial EST sequence (1-t-12)
2	CATGATTTGAGAAC	H260227	603	566	158	249	173	F12396	H.sapiens partial cDNA sequence; clone c-39e04.
3	CATGTGATTTCACCT	H933704	452	595	235	80	314	L08441	Human autonomously replicating sequence (ARS) mRNA
4	CATGTTTCATACACCT	H1002566	444	357	114	64	191	F15553	H.sapiens mitochondrial EST sequence (001T14)
5	CATGCCACTGCACCTC	H335432	385	402	223	278	132	X51525	Human cortex mRNA containing an Alu repetitive element
6	CATGACTAACACCCCT	H114966	369	446	171	76	161	F16402	H.sapiens mitochondrial EST sequence (141-20)
7	CATGCACTACTCACC	H291282	293	527	78	14	83	U09500	Human mitochondrion cytochrome b gene, partial cds
8	CATGAAAACATTCTC	H1272	200	169	98	17	223	F15744	H.sapiens mitochondrial EST sequence (101-03)
9	CATGCTCATAAGGAA	H478249	184	127	70	21	75	F15511	H.sapiens mitochondrial EST sequence (1-t-07)
10	CATGTCGAAGCCCC	H885334	147	183	94	49	57	F18587	H.sapiens mitochondrial EST sequence (022T19)
11	CATGACGCGAGGAGA	H103075	145	160	91	69	47	H03983	y47a08.s1 Homo sapiens cDNA clone 151862 3'
12	CATGTTGGCCAGGCT	H1025322	124	194	63	111	51	X74301	H.sapiens mRNA for MHC class II transactivator.
13	CATGTTGGTGAAAGGA	H1027595	98	106	17	183	107	M17733	Human thymosin beta-4 mRNA, complete cds.
14	CATGATCACGCCCTC	H214616	97	186	17	41	49	U46913	Human EST overexpressed in pancreatic cancer (xs31)
15	CATGTGCCTGCACCA	H941638	67	48	25	75	34	X05607	Human mRNA for cysteine proteinase inhibitor precursor
16	CATGAGACCCACAAC	H136465	64	121	28	24	15	D54113	Human fetal brain cDNA 5'-end GEN-129B05.
17	CATGAGTTTGTAGT	H196339	60	33	17	13	15	X14758	Human mRNA for adenocarcinoma-associated antigen
18	CATGGGAACAAACAG	H656389	56	41	4	31	3	L33930	Homo sapiens CD24 signal transducer mRNA
19	CATGGTGGTGATGCA	H965434	53	271	6	30	5	D50954	Human fetal brain cDNA 3'-end GEN-002A10.
20	CATGGAATACAGTT	H527436	49	35	10	100	36	M11233	Human cathepsin D mRNA, complete cds.
21	CATGGTGGTCACGC	H763719	49	37	21	27	15	U25801	Human Tax1 binding protein mRNA, partial cds.
22	CATGGTGGTGACAC	H765509	45	26	18	23	15	U31215	Human metabotropic glutamate receptor 1 alpha
23	CATGGGGTTGGCTTG	H704160	44	56	2	6	1	S79597	tRNA ^{Ser} (UNC) [human, muscle, MERRF/MELAS overlap s
24	CATGGTGGCGGTGC	H763567	42	32	15	20	5	T48809	yb05c03.r1 Homo sapiens cDNA clone 70276 5' contai
25	CATGTAGACTAGCAA	H821029	39	23	1	23	10	M69023	Human globin gene.

26	CATGGCTAGGTTTAT	H641789	38	144	13	25	13	D51017	Human fetal brain cDNA 3'-end GEN-007C04.
27	CATGGGCTTTAGGGA	H687915	37	372	6	29	11	W15552	zb91h1.s1 Soares parathyroid tumor NbHPA Homo sap
28	CATGGGGGTCAGGG	H699691	37	170	11	16	9	F16326	H.sapiens mitochondrial EST sequence (132-20) from skeletal muscle
29	CATGATTTTCTAAAA	H261569	33	13	11	8	2	AA315049	EST18695 HCC cell line (metastasis to liver in mouse) II Homo sapiens cDNA 5' end
30	CATGCACTTGCCCT	H294488	33	18	11	17	36	F01150	H. sapiens partial cDNA sequence; clone A6A03; ver
31	CATGCCCTGCTGCAGG	H386963	32	13	0	6	2	N29971	yw53h01.s1 Homo sapiens cDNA clone 255985 3'
32	CATGAGAACTTCCA	H132598	32	14	3	16	12	K02883	Human MHC class I HLA-A2 gene, complete cds.
33	CATGCTCTGCCCTC	H489822	32	32	7	20	5	R09140	yf25f12.s1 Homo sapiens cDNA clone 127919 3'
								R76005	yf22c10.s1 Homo sapiens cDNA clone 158954 3'
								T33596	EST38371 Homo sapiens cDNA 3' end similar to None..
34	CATGGCCATCCCTT	H609624	29	73	7	14	16	F16449	H.sapiens mitochondrial EST sequence (129-09)
35	CATGGCCACGCGGCC	H610922	28	9	1	1	7	AA292959	z54f10.s1 Soares ovary tumor NbHOT Homo sapiens cDNA clone 726187 3'
36	CATGTGGCGGTGTC	H956860	26	8	1	1	2	AA292466	z31c11.r1 Soares ovary tumor NbHOT Homo sapiens cDNA clone 723956 5' similar to TR:G205858 G205858 RAT ORF
								N92384	zb62d07.s1 Soares fetal lung NbHL19W Homo sapiens cDNA clone 308173 3' similar to PIR:A39484 A39484 androgen-withdrawal apoptosis protein RVPI, prostatic - rat
									zb19c06.s1 Homo sapiens cDNA clone 302506 3' similar to PIR:A39484 A39484 androgen-withdrawal apoptosis protein RVPI, prostatic - rat ;
								N80203	zk39d06.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 485195 3' similar to PIR:A39484 A39484 androgen-withdrawal apoptosis protein RVPI
37	CATGAGGGTGTTTTC	H175872	26	218	7	20	10	AA039323	Human partial cDNA sequence with CCA repeat region
38	CATGCCCTGGGAAGTG	H387596	25	10	0	45	17	U21468	Human epistatin variant A mRNA, 3' end.
39	CATGAGTCTGCTGGA	H188027	24	9	1	0	0	M34088	Unknown
40	CATGCCCGCCTCTTC	H353760	24	11	2	3	4	T10098	seq816 Homo sapiens cDNA clone b4HB3MA-COT8-HAP-Ft
41	CATGAAAAAGAGTGGT	H2235	22	9	2	0	7	X83228	H.sapiens mRNA for LI-cadherin.
42	CATGGCCACGTGGAG	H607977	21	7	1	2	2	L27415	Homo sapiens huntingtin (HD) gene, exon 66.
43	CATGAGGATGTGGG	H167659	21	5	4	1	3	C00470	dbj C00470 C00470 HUMGS0007620, Human Gene Signature, 3'-directed cDNA sequence.
								yy62g08.s1 Homo sapiens cDNA clone 278174 3'.	

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62	CATGGGGCTACGTCC	H695406	14	4	0	1	0	M25629	Human kallikrein mRNA, complete cds, clone clone p
63	CATGCCCGGCTCCTC	H354776	14	7	1	5	2	H18836	ym45d10.s1 Homo sapiens cDNA clone 51262 3'
								AA026974	zk01e10.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 469290 3'
								AA405031	zu12c12.r1 Soares testis NHT Homo sapiens cDNA clone 731638 5' similar to gb:M61900 Human prostaglandin D synthase gene, complete cds. (HUMAN);
64	CATGAGGTACTACTA	H176584	13	9	0	9	8	U66894	gb U66894 HSU66894 Human epithelium-restricted Ets protein ESX mRNA;
								U73843	Human epithelial-specific transcription factor ESE-1b (ESE-1) mRNA, complete cds
65	CATGCAAAATAAATTA	H265232	13	3	0	1	0	D25996	Human colon 3'directed Mbol cDNA, HUMGS06772
66	CATGCTGTAAAAAAA	H503809	13	6	0	1	1		Unknown
67	CATGGTTCAATCCCT	H774358	13	3	0	2	0	AA071520	ze88g07.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 366108 3'
								N90742	za90h10.s1 Soares fetal lung NbHL19W Homo sapiens cDNA clone 299875 3'
								AA086292	zn52h06.s1 Stratagene muscle 937209 Homo sapiens cDNA clone 561851 3'
68	CATGAATAAAGCCTT	H49304	12	4	0	0	0	D11499	Human HepG2 3'-directed Mbol cDNA, clone a-35.
69	CATGGGAAGTTTAC	H658173	12	2	0	1	0	T16031	IB2474 Homo sapiens cDNA 3'end.
70	CATGGGATGGCTTAT	H670333	12	1	0	6	1	T74426	yc82e01.r1 Homo sapiens cDNA clone 22306 5'.
71	CATGGGTGGCCCGGG	H715099	12	2	0	3	2	N73771	za61h02.s1 Homo sapiens cDNA clone 297075 3'.
								W90388	zh75T08.s1 Soares fetal liver spleen 1NFLS S1 Homo sapiens cDNA clone 417927 3'
								F03786	H. sapiens partial cDNA sequence; clone c-29h08.
72	CATGTACTGTACTTC	H817952	12	2	0	0	0	U14631	Human 11 beta-hydroxysteroid dehydrogenase type II
73	CATGCCCTTGCACTC	H360008	11	6	0	3	3	T41121	ya31a06.s5 Homo sapiens cDNA clone 62194 3' contains Alu repetitive element.
74	CATGCGGTGGGACCA	H440966	11	4	0	2	0		Unknown
75	CATGGCCCCCAACCA	H611590	11	2	0	0	0		Unknown
76	CATGGCCGGCGCTC	H616862	11	2	0	0	0	Z58486	Unknown
77	CATGGGAGGGCGCTCA	H666014	11	1	0	0	0		Unknown

78	CATGTCCTCCCGTTACA	H874226	11	11	0	0	0	0	W68073	zd42c12.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 343318 3' similar to contains Alu repetitive element;
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Table 4 - Transcripts increased in pancreas_cancer -
SAGE Tags elevated only in Pancreatic Tumor

NC Normal Colon
 Tu Colon Tumor
 CC Colon Cancer Cell Line
 PT Pancreatic Tumor
 PC Pancreatic Cell Line

	Tag Sequence	Tag Number	NC	Tu	CC	PT	PC	Examples	Accession	Gene Name
1	CATGAAGCAACCA	H9222	0	6	1	3	11	Examples	R38305	yh95b04.s1 Homo sapiens cDNA clone 137455 3'
									AA126719	zk95b03.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 490541 3'
									AA044296	zk51c03.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 486340 3'
									AA131586	zl33c08.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 503726 3'
									AA157983	zo71h12.s1 Stratagene pancreas (#937208) Homo sapiens cDNA clone 592391 3'
2	CATGAAGCAGTTTA	H9408	1	5	2	21	3	Examples	AA292929	zl54e04.s1 Soares ovary tumor NbHOT Homo sapiens cDNA clone 726174 3'
									AA159306	zo78c07.s1 Stratagene pancreas (#937208) Homo sapiens cDNA clone 154129 3'
									R54012	yy70h01.s1 Homo sapiens cDNA clone 154129 3'
									T62936	yb99f08.s1 Homo sapiens cDNA clone 79335 3'
									X52426	H. sapiens mRNA for cytokeratin 13
3	CATGAAGCGGGCT	H9898	0	0	0	0	13	Examples	X51698	H. sapiens spasmolytic polypeptide (SP) mRNA.
4	CATGAATCCTGGGT	H13803	0	1	1	16	2	Examples	N70419	za61d12.s1 Homo sapiens cDNA clone 297047 3'
5	CATGAATGGACAC	H14865	0	0	1	0	13	Examples	AA411599	zv16g01.r1 Soares NbHPu S1 Homo sapiens cDNA clone 753840 5'
									AA410508	zv16g01.s1 Soares NbHPu S1 Homo sapiens cDNA clone 753840 3'
									AA115723	zl86g12.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 511558 3'
6	CATGAACAGTTTGT	H21247	1	1	6	8	13	Examples	AA132875	zo19c04.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 587358 3'
									AA147677	zo44a06.s1 Stratagene endothelial cell 937223 Homo sapiens cDNA clone 589714 3'

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23	CATGACTCAGCCGG	H119383	0	0	3	21	3	Examples	M92357	Homo sapiens B94 protein mRNA, complete cds.
24	CATGACTGAGGAAG	H123521	0	0	0	53	22	Examples	X64875	H. sapiens mRNA for insulin-like growth factor binding protein 3
									M31159	Human growth hormone-dependent insulin-like growth factor binding protein 3
									M33878	Human insulin-like growth factor-binding protein-3
									S56205	insulin-like growth factor binding protein 3 (3' region)
25	CATGACTGCCGCTG	H124264	1	0	0	22	9	Examples	U65932	Human extracellular matrix protein 1 (ECM1) mRNA
									U65937	Human extracellular matrix protein 1 (ECM1) gene, exon 9
									zo03f09.s1	Stratagene colon (#937204) Homo sapiens cDNA clone 566633
26	CATGACTGTATTTTC	H126208	3	4	9	2	22	Examples	AA148916	3'
									AA129137	zo12a11.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 586652
									AA115437	3'
									AA126967	2185g09.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 511456
									AA126967	3'
27	CATGAGCACTGCAGC	H149395	1	2	6	3	16	Examples	R24613	2187e07.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 511620
28	CATGAGCAGGAGCGT	H150055	1	0	0	0	15	Examples	H43243	3'
29	CATGAGCTGTATTCT	H162622	0	2	0	1	11	Examples	X54942	yh36c03.r1 Homo sapiens cDNA clone 131812
									AA044081	yp05e05.r1 Homo sapiens cDNA clone 186560 5'
30	CATGAGGATGACCCC	H167446	1	7	12	10	13	Examples	AA044081	H. sapiens ckshs2 mRNA for Cks1 protein homologue
									AA044211	zk50g07.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 486300 3'
									AA044211	486300 5' similar to PIR: A40533 A40533 cAMP-dependent protein kinase major membrane substrate
31	CATGAGGCTCTCAAT	H178129	4	2	0	60	2	Examples	X14787	Class A, Human mRNA for thrombospondin.
32	CATGAGGTGCGGGG	H178603	0	2	2	1	11	Examples	R27738	yh64f11.s1 Homo sapiens cDNA clone 134541 3'
									H00276	y122f12.s1 Homo sapiens cDNA clone 149519 3' similar to SP:ZK637.5
									CE00436 ARSA	CE00436 ARSA
33	CATGAGTATCTGGGA	H183787	3	3	1	15	73	Examples	AA076235	zm19d07.s1 Stratagene pancreas (#937208) Homo sapiens cDNA clone 526093 3'
									H13159	y116c04.s1 Homo sapiens cDNA clone 148902 3'
									AA146632	zo71e11.s1 Stratagene pancreas (#937208) Homo sapiens cDNA clone 592364 3'
34	CATGATACTTTAATT	H204740	1	0	3	18	9	Examples	X80062	H. sapiens SA mRNA
									U01691	Human annexin V (ANX5) gene

47	CATGCAGCCTGGGGC	H300971	0	0	0	0	0	0	10	Examples	AA149942	2068d04.s1 Stratiogene pancreas (#937208) Homo sapiens cDNA clone 592039 3' similar to TR.E218488 E218488 TRYPTASE
48	CATGCAGCGGCCCT	H301462	4	11	12	10	21			Examples	AA187553	zp66b09.r1 Stratiogene endothelial cell 937223 Homo sapiens cDNA clone 625145 5' similar to gb.M16937 HOMEBOX PROTEIN HOX-B7 (HUMAN); contains element MER22 repetitive element
49	CATGCAGGTTGTCCT	H307126	0	0	4	0	10			No Match	M16937	Homeobox protein HOX-B7
50	CATGCAGTCTCTCAA	H309109	2	6	6	2	17			Examples	U14972	Human ribosomal protein S10 mRNA
51	CATGCATCCGTGAC	H316857	0	3	3	3	13			Examples	U72793	Human leukotriene A4 hydrolase gene
											J03459	Human leukotriene A-4 hydrolase mRNA, complete cds
											J02959	Human leukotriene A-4 hydrolase mRNA, complete cds
52	CATGCATTCTCCTT	H325080	0	2	5	13	3			Examples	X82434	H. sapiens mRNA for enterin
53	CATGCCACCCACC	H333138	3	7	17	18	2			Examples	M88338	Human serum constituent protein (MSE55) mRNA
54	CATGCCAGTGGCCCG	H339606	23	11	37	22	56			Examples	U14971	Human ribosomal protein S9 mRNA
55	CATGCCATTTCTGG	H344031	0	2	6	1	10			Examples	L01697	Homo sapiens alpha-1 type XV collagen mRNA
56	CATGCCCAAGCTAGC	H344691	19	8	8	18	44			Examples	X34079	Human mRNA for heat shock protein HSP27.
											Z23090	H. sapiens mRNA for 28 kDa heat shock protein
											X16477	Human mRNA fragment for estrogen-regulated 24k protein
											S74571	estrogen receptor-related protein=27-kDa heat shock protein
57	CATGCCCATCCGAAA	H347489	20	15	43	19	61			Examples	X69392	H. sapiens mRNA for ribosomal protein L26.
											L07287	Human ribosomal protein L26 (RPL26) gene
58	CATGCCCCCTGCAGA	H350099	0	1	6	14	25			Examples	U40434	Human mesothelin or CAK1 antigen precursor mRNA
											D49441	Human mRNA for pre-pro-megakaryocyte potentiating factor, complete cds.
59	CATGCCCGCATAGAT	H353481	0	0	0	8	11			Examples	U12819	Human p16-INK4 (p16) gene
											U38945	Human hypothetical 18.1 kDa protein (CDKN2A) mRNA
											S69804	MTS1= multiple tumor suppressor 1/cyclin-dependent kinase 4 inhibitor p16
											S69822	CDK4=cyclin-dependent kinase 4 inhibitor
											S78535	tumor suppressor gene, P16/MTS1/CDKN2=cell cycle negative regulator beta form
60	CATGCCCTCCTGGGG	H357867	8	2	5	14	34			Examples	Z47319	H. sapiens mRNA for expressed sequence tag (clone 2167119)

										AA398406						zif60hl2.s1 Soares testis NHT Homo sapiens cDNA clone 726791 3'
										U21049	Examples	4	1	14	19	Human DD96 mRNA
61	CATGCCGGCCGTACC	H370034	4	4	1	14	19			XO3212	Examples	0	2	1	30	KERATTIN, TYPE II CYTOSKELETAL 7
62	CATGCTCGTGCCCAG	H387925	0	2	1	30	99									zp7f3f0l.s1 Stratagene HeLa cell s3 937216 Homo sapiens cDNA clone 625849 3'
										AA187637						zp35g11.s1 Stratagene muscle 937209 Homo sapiens cDNA clone 611492 3' similar to TR: G663269 G663269 BOLA
63	CATGCCTTTGAACAG	H392709	5	3	6	2	23			AA176457	Examples					zp35e11.s1 Stratagene muscle 937209 Homo sapiens cDNA clone 611468 3' similar to TR: G663269 G663269 BOLA.
										AA176541						Human interferon-inducible mRNA fragment
64	CATGCCCGCAGCATG	H415844	21	13	45	75	7			XO2492	Examples					ya88g05.s1 Homo sapiens cDNA clone 68792 3'
65	CATGCTCAACAGCAA	H475429	2	5	10	6	17			T53402	Examples					zd47g08.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 343838 3' similar to PIR:S24168 S24168 hypothetical protein - human
										W69493						Human mRNA for LDL-receptor related protein
66	CATGCTCAACCCCC	H475478	1	4	2	23	1			X13916	Examples					H.sapiens (24) Ferritin H pseudogene.
67	CATGCTGAGAATACTG	H493576	2	3	1	8	18			X80335	Examples					Human mRNA for G(i) protein alpha-subunit
68	CATGCTGAGTCCTCC	H494454	1	4	4	21	13			X04828	Examples					Human ribosomal protein L5 mRNA
69	CATGCTGCTATACGA	H498887	16	30	28	30	44			UI14966	Examples					ydlglg08.s1 Homo sapiens cDNA clone 110846 3'
70	CATGCTGCTGAGTGA	H499247	1	3	4	13	13			T90665	Examples					EST473791 Fetal brain I Homo sapiens cDNA 3' end similar to steroid hormone receptor hERR1
										AA338799						yv98b06.s1 Homo sapiens cDNA clone 250739 3'
										H97236						Human fetal brain cDNA 3'-end GEN-018D10
71	CATGCTGGCGCCGAT	H501337	0	0	4	0	10			C14084	Examples					Human lipocortin II mRNA
72	CATGCTTCCAGCTTA	H513181	64	23	36	53	104			D00017	Examples					H.sapiens gene for cytokeratin 17.
73	CATGCTTCTTGCCT	H514022	0	3	4	89	7			Z19574	Examples					H.sapiens mRNA for keratin-related protein
										X62571						H.sapiens radiated keratinocyte mRNA 266
										X03803						Human ERF-J mRNA 3' end.
74	CATGCTTCTTCCCT	H522198	0	2	1	16	4			X79067	Examples					Human mRNA containing an Alu repeat
75	CATGGAAAAA	H524289	7	14	21	26	37			X51779	Examples					H.sapiens mRNA for T-cell leukemia lymphoma 1
76	CATGGAAAACAAGATG	H525348	4	7	14	8	22			X82240						Human mRNA encoding phosphoglycerate kinase.
										V00572	Examples					Human keratinocyte cDNA, clone 001
										D29018						Human phosphoglycerate kinase (pgk) mRNA
										L00160						Human mRNA for cathepsin D
77	CATGGAATAACAGTT	H527436	49	35	10	100	36			X05344	Examples					

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11	CATGGTGGGAGAT	H715401	1	4	10	10	14	Examples	J00202	human bla-dr heavy chain gene; 3' flank
12	CATGGTCTGTGAGCA	H728778	3	3	1	16	30	Examples	U18009	Human chromosome 17q21 mRNA clone LF113.
123	CATGGTACTGTGGCT	H728810	23	10	16	15	50	Examples	T33413	EST57778 Homo sapiens cDNA 3' end similar to None
124	CATGGTCAAAATTC	H737344	0	0	0	10	1	Examples	T33339	EST57474 Homo sapiens cDNA 3' end similar to None
125	CATGGTCTGGGGCTT	H752296	25	35	45	76	29	Examples	M59911	Human integrin alpha-3 chain mRNA
126	CATGGTCTGTGAGAG	H752521	0	5	7	12	2	Examples	X87689	H. sapiens mRNA for putative p64 CLCP protein
127	CATGGTCTGTGAGG	H752531	0	0	0	1	13	No Match	L12350	Human thrombospondin 2 (THBS2) mRNA
128	CATGGTCTTGAAGCC	H753162	0	1	2	1	10	No Match	D21261	Human mRNA (HA1756) for ORF
129	CATGGTGAAGGCGAGT	H754323	25	14	42	15	89	Examples	D29543	Human keratinocyte cDNA, clone 686
130	CATGGTGAATGACGG	H754567	0	2	8	1	10	Examples	H51290	yp07a05.s1 Homo sapiens cDNA clone 186704 3'
131	CATGGTGGGAGGAC	H760361	0	3	2	11	25	Examples	N20338	yx44g12.s1 Homo sapiens cDNA clone 264646 3'
132	CATGGTGGCTGGAGAA	H761481	2	9	9	13	26	Examples	AA158271	zo76e09.s1 Stratagene pancreas (#937208) Homo sapiens cDNA clone 592840 3'
133	CATGGTGGAGGCAC	H762533	1	1	3	6	34	Examples		
134	CATGGTGGTACAGGA	H765003	14	17	15	39	30	Examples		
135	CATGGTTCACTGCAG	H774629	0	2	1	13	3	Examples	AA047563	376786 3'
136	CATGGTTGTCTTTGG	H781823	1	1	6	30	24	Examples	AA130701	zo13f02.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 586779
137	CATGGTTGTGGTTAA	H782013	178	110	14	340	139	Examples	X59288	3'
138	CATGGTTTAAATCGA	H782391	1	6	12	4	14	Examples	M24283	H. sapiens gene for intercellular adhesion molecule
139	CATGTAAGGCTTAAC	H797169	0	0	6	1	12	Examples	J03132	Human major group rhinovirus receptor (HRV) mRNA
140	CATGTAATTTTGGA	H802793	0	2	5	2	10	No Match	M55100	Human intercellular adhesion molecule-1 (ICAM-1)
										Human cell surface glycoprotein P3.58 mRNA
										Human complement component C3 mRNA, alpha and beta
										Human beta-2-microglobulin gene
										Human mRNA for proteasome subunit HC3
										INSULIN-LIKE GROWTH FACTOR IA PRECURSOR (HUMAN)

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158	CATGTGATGTCGGT	H932731	0	8	3	11	12	Examples	AA077860	2k03h07.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 469693 3'
159	CATGTGGCATCTGTA	H938876	1	3	7	3	16	Examples	M25753	G2MITOTIC-SPECIFIC CYCLIN B1 (HUMAN)
									T60151	yc22c04.s1 Homo sapiens cDNA clone 81414 3'
									R67969	yl29g08.s1 Homo sapiens cDNA clone 140702 3'
										2o91f03.s1 Stratagene ovarian cancer (#937219) Homo sapiens cDNA clone 594269 3' similar to SW:NGAL_HUMAN P80188 NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN PRECURSOR
160	CATGTGCCCTCAAAA	H939841	11	13	3	13	43	Examples	AA169614	2b15d08.s1 Homo sapiens cDNA clone 30217 3' similar to SW:NGAL_HUMAN P80188 NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN PRECURSOR
161	CATGTGCCCTCAGAA	H939849	3	4	0	11	19	Examples	N79823	zm90h04.s1 Stratagene ovarian cancer (#937219) Homo sapiens cDNA clone 545239 3' similar to SW:NGAL_HUMAN P80188 NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN PRECURSOR
162	CATGTGCCCTCAGGA	H939851	13	31	10	25	83	Examples	AA075896	zl81e07.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 511044 3'
162	CATGTGCCCTCAGGC	H920192						No Match		
163	CATGTGCCCTTACTTT	H941856	0	3	1	2	12	Examples	AA100279	
164	CATGTGCGCTGGCCC	H944038	2	5	2	17	3	No Match		zk10a01.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 470088 3'
165	CATGTGCTTCATCTG	H949560	2	6	6	4	16	Examples	AA029262	yv66e10.s1 Soares fetal liver spleen INFLS Homo sapiens cDNA clone 247722 3'
									N54281	zn76c02.s1 Stratagene NT2 neuronal precursor 937230 Homo sapiens cDNA clone 564098 3'
									AA114075	Homo sapiens guanylate kinase (GUK1) mRNA
166	CATGTGGAGTGAGG	H953251	18	15	7	22	48	Examples	L76200	Human mRNA for precursor of apolipoprotein C1
167	CATGTGGCCCCAGGT	H955723	0	3	3	37	4	Examples	X00570	Homo sapiens cathepsin B mRNA
168	CATGTGGGTGAGCCA	H962086	13	15	13	76	27	Examples	L16510	Human cathepsin B proteinase mRNA, complete cds
									M14221	Human enigma gene
169	CATGTGTGAGCCCT	H975446	3	3	3	22	8	Examples	L35240	Homo sapiens ribosomal protein L34 (RPL34) mRNA
170	CATGTGTGCTAAATG	H976644	8	21	26	18	50	Examples	L38941	Human gene for histone H1(O)
171	CATGTGTGTGTGT	H978687	6	7	16	25	15	Examples	X03473	2k23g08.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 471422 3'
172	CATGTGTATGGATCTC	H997944	0	1	1	21	1	Examples	AA034505	

																			z131b06.s1 Soares ovary tumor NbHOT Homo sapiens cDNA clone 723923 3'	
																			AA235464	zk30c10.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 472030 3'
																			AA037024	yv38d04.s1 Homo sapiens cDNA clone 236071 3'
																			H53629	EST04595 Homo sapiens cDNA clone HFBDX32
																			T06706	
																				NIB1599 Normalized infant brain, Bento Soares Homo sapiens cDNA 3'end similar to EST04595 H. sapiens cDNA clone HFBDX32
																			T16635	ze97h02.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 366963 3'
																			AA026678	zi05a03.s1 Soares NbHTGBC Homo sapiens cDNA clone 712204 3'
																			AA280283	ym05a09.s1 Homo sapiens cDNA clone 46675 3'
																			H10141	H.sapiens mRNA for tyrosine kinase receptor
																			X66029	Human mRNA for collagen VI alpha-1
																			X15880	H.sapiens gene for glutaminyl-tRNA synthetase
																			X72414	zk73h10.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 488515 3'
																			AA044568	yz36b07.s1 Homo sapiens cDNA clone 285109 3'
																			N71899	zi71g03.s1 Soares testis NHT Homo sapiens cDNA clone 727828 3'
																			AA400793	H.sapiens (5) Ferritin H pseudogene.
																			X80336	Human mRNA for apoferritin H chain type
																			X00318	Human apoferritin H gene exons 2-4
																			X03488	Human ferritin heavy chain mRNA, complete cds
																			M97164	Human ferritin heavy chain mRNA, complete cds
																			L20941	Human interferon-inducible mRNA (cdNA 6-26).
																			X02493	Human promyelocytic leukemia cell mRNA
																			M11948	Human thymosin beta-4 mRNA, complete cds
																			M17733	Human thymosin beta-4 mRNA, complete cds
																			N78832	zb17a08.s1 Homo sapiens cDNA clone 302294 3'
																			Examples	zz33d02.s1 Soares ovary tumor NbHOT Homo sapiens cDNA clone 724131 3'
																			AA411095	3'
																			W81693	zd84gl1.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 347396 3'

S1	CATGTTTCCTTCCTT	H1038296	0	6	3	7	17	Examples	M20471	Human brain-type clathrin light-chain A mRNA
									M20472	Human lymphocyte clathrin light-chain A mRNA
S2	CATGTTTGACCTTT	H1041504	2	0	0	16	1	Examples	X78947	H. sapiens mRNA for connective tissue growth factor
									U14750	Human connective tissue growth factor mRNA
									H06492	yl78c08.s1 Homo sapiens cDNA clone 44273 3'
S3	CATGTTTGTTAAA	H1044225							T35952	EST94173 Homo sapiens cDNA 3' end similar to None
									AA253218	z53g10.s1 Soares NhHMPu S1 Homo sapiens cDNA clone 667170 3'

Table 5 - Transcripts increased in pancreas and colorectal cancer
 SAGE tag that were elevated in both in colorectal and pancreatic tumor,
 and are likely to be specific for tumor in general.

Tag Sequence	Tag Number	Accession	Description
1 CATG TGAATGAC C	-950498	M10629	Human alpha-1 collagen gene, 3' end with polyA sit
2 CATG CACTTCAAGG G	-294155	U42376	Human retinoic acid induced RIG-E precursor (E) mR
		U56145	Human thymic shared antigen-1/stem cell antigen-2
3 CATG ATGTGAAGAG T(A)	-243747	J03040	Human SPARC/osteonectin mRNA, complete cds.
		M25746	Human osteonectin gene exon 10, complete cds.
4 CATG GCCCAAGGAC C	-610466	X53416	Human mRNA for actin-binding protein (filamin) (AB
5 CATG ATCTTGTAC T	-229106	X02761	Human mRNA for fibronectin (FN precursor).
		K00799	human fibronectin (fn) 3' coding region and flank,
6 CATG GTGGCTGAG C	-760291	X58536	Human mRNA for HLA class I locus C heavy chain.
		M26432	Human MHC class I HLA-C.1 gene, complete cds.
7 CATG ACAGGCTACG G	-762311	M95787	Human 22kDa smooth muscle protein (SM22) mRNA, com
		M83106	Human SM22 mRNA, 5' end.
8 CATG GTGTGTTGT A	-769020	M77349	Human transforming growth factor-beta induced gene
9 CATG GATTCTCAG C	-589267	X53279	Human mRNA for placental-like alkaline phosphatase
		X55958	H.sapiens mRNA for alkaline phosphatase.
		J04948	Human alkaline phosphatase (ALP-1) mRNA, complete
10 CATG ACCATTCTGC T	-85882	X57351	Human 1-8D gene from interferon-inducible gene fam
		X02490	Human interferon-inducible mRNA (cDNA 1-8).
			Human mRNA for alpha-actinin.
11 CATG TCCTTCTCCA C	-884181	X15804	Human mRNA for KIAA0190 protein.
12 CATG CTTCTGTGTA C,T	-515821	D80012	Human TB2 gene mRNA, 3' end.
13 CATG ATGTAAAAA T	-241665	M74090	Human lysozyme mRNA, complete cds with an Alu repe
		J03801	Human lysozyme mRNA, complete cds.
		M19045	Human lysozyme mRNA, complete cds.
14 CATG GGCAGAGGAC C	-673954	X17620	Human mRNA for Nm23 protein, involved in developme
		X75598	H.sapiens nm23H1 gene.
			Human Int-6 mRNA, complete cds.
15 CATG AATATTGAGA A	-53129	U62962	Human HepG2 3' region cDNA, clone hmd2c11.
16 CATG TTTTGTATAA A	-1048113	D16891	Human HepG2 3' region cDNA, clone hmd2c11.
17 CATG CAGCTGGCCA T	-302741	X53743	H.sapiens mRNA for fibulin-1 C.

18	CATG GTTCACATTA	G	-774461	X00497	Human mRNA for HLA-DR antigens associated invariant
				M13560	Human Ia-associated invariant gamma-chain gene, ex
19	CATG AAAAGAACT	T	-2056	Y00345	Human mRNA for polyA binding protein.
20	CATG AATGCAGCA	G	-58533	M61831	Human S-adenosylhomocysteine hydrolase (AHCY) mRNA
				M61832	Human S-adenosylhomocysteine hydrolase (AHCY) mRNA
21	CATG TGAATAAAA	C	-918273	X16934	Human HB23 gene for B23 nucleophosmin.
				M28699	Homo sapiens nucleolar phosphoprotein B23 (NPM1) m
				M23613	Human nucleophosmin mRNA, complete cds.
				M26697	Human nucleolar protein (B23) mRNA, complete cds.
22	CATG TTATGGATC	T	-998030	M24194	Human MHC protein homologous to chicken B complex
23	CATG CAATAATGT	T	-274492	D23661	Human mRNA for ribosomal protein L37, complete cds
				L11567	Homo sapiens ribosomal protein L37 mRNA, complete
24	CATG AGCCTTGTG	G	-155632	D83174	Human mRNA for collagen binding protein 2.
25	CATG ACCTGTATCC	C	-97078	X57352	Human 1-8U gene from interferon-inducible gene fam
26	CATG TTCAATAAAA	A	-1000193	M17886	Human acidic ribosomal phosphoprotein P1 mRNA, com
				J05068	human transcobalamin I mRNA, complete cds.
27	CATG CGACCCACG	C	-398663	M12529	Human apolipoprotein E mRNA, complete cds.
				K00396	Human apolipoprotein E (epsilon 2 and 3 alleles) m
28	CATG CAGATCTTTG	T	-298495	X56998	Human Uba52 adrenal mRNA for ubiquitin-52 amino ac
				X56999	Human Uba52 placental mRNA for ubiquitin-52 amino
29	CATG CTGGCGGCG	C	-501287	X07491	Human DNA inserts showing sperm-specific hypomethy
				M91670	Human ubiquitin carrier protein (E2-EPPF) mRNA, com
30	CATG ATTGGCTTAA	A	-256497	L14272	Human prohibitin (PHB) gene, exons 1-7.
				S85655	prohibitin [human, mRNA, 1043 nt].
31	CATG GTGGTGGACA	C	-765573	U62435	Human nicotinic acetylcholine receptor alpha6 subu
				U68041	Human breast and ovarian cancer susceptibility pro
32	CATG TCCTGCCCCA	T	-883029	M24398	Human parathymosin mRNA, complete cds.
33	CATG ACTGGGTCTA	T	-125661	X58965	H. sapiens RNA for nm23-H2 gene.
				M36981	Human putative NDP kinase (nm23-H2S) mRNA, complet
				L16785	Homo sapiens c-myc transcription factor (puf) mRNA
34	CATG AAGAAGATAG	A	-33331	U02032	Human ribosomal protein L23a mRNA, partial cds.
				U37230	Human ribosomal protein L23a mRNA, complete cds.
				U43701	Human ribosomal protein L23a mRNA, complete cds.

			L13799	Homo sapiens (clone 01) liver expressed protein mR
			L06505	Human ribosomal protein L12 mRNA, complete cds.
35	CATG ACATCATCGA	T	-79065	Human ribosomal protein L12 mRNA, complete cds.
36	CATG CTGTTGGTGA	T	-507577	Human homolog of yeast ribosomal protein S28, comp
37	CATG ATTATTTTC	T	-249854	H. sapiens mRNA for ribosomal protein L7.
			X57959	H. sapiens mRNA for ribosomal protein L7.
			X57958	H. sapiens mRNA for ribosomal protein L7.
			X52967	Human mRNA for ribosomal protein L7.
			L16558	Human ribosomal protein L7 (RPL7) mRNA, complete c
			L06498	Homo sapiens ribosomal protein S20 (RPS20) mRNA, c
38	CATG GCITTTAAGG	A	-655115	Homo sapiens ribosomal protein L27 (RPL27) mRNA, c
39	CATG GGCAGAAGA	A	-672265	Homo sapiens ribosomal protein L27 (homologue of r
			L25346	Homo sapiens ribosomal protein L27 (homologue of r
			Y00433	Human mRNA for glutathione peroxidase (EC 1.11.1.9
40	CATG CTCITCGAGA	A	-490889	Human gene for glutathione peroxidase.
			Y00483	Human gene for glutathione peroxidase.
			X13710	H. sapiens unsplined mRNA for glutathione peroxidase
			X13709	Human gpx1 mRNA for glutathione peroxidase.
			M21304	Human glutathione peroxidase (GPX1) mRNA, complete
			X04347	Human liver mRNA fragment DNA binding protein UPI
41	CATG CTGTTGATTG	C	-507455	Human clone C4E 3.2 (CAC)n/(GTG)n repeat-contains
			U00947	Human clone C4E 3.2 (CAC)n/(GTG)n repeat-contains
			M81757	H. sapiens S19 ribosomal protein mRNA, complete cds
42	CATG CTGGGTTAAT	A	-502724	Human mRNA for LRep3.
43	CATG ATGCTGGTA	T	-239533	Human mRNA for Epstein-Barr virus small RNAs (EBER
44	CATG GATGCTGCCA	A	-583573	Human mRNA for Epstein-Barr virus small RNAs (EBER
			L21756	Homo sapiens acute myeloid leukemia associated pro
			D17652	Human mRNA for HBP15/L22, complete cds.
			S76343	AML1...EAP (translocation breakpoint) [human, chro
			U14970	Human ribosomal protein S5 mRNA, complete cds.
45	CATG CCTTCGAGAT	C	-390692	Human Bak mRNA, complete cds.
46	CATG CTCCTCACCT	G	-482584	Human Bak protein mRNA, complete cds.
			U23765	Human mRNA for elongation factor 1-alpha (clone CE
47	CATG TGTGTTGAGA	G	-978825	Human DNA for elongation factor 1-alpha (clone lam
			X16872	Human mRNA for elongation factor 1 alpha subunit (
			X03558	Human HepG2 3' region MboI cDNA, clone hmd2h03m3.
			D17182	Human HepG2 3' region MboI cDNA, clone hmd4h05m3.
			D17245	Human HepG2 3' region MboI cDNA, clone hmd5d07m3.
			D17259	Human HepG2 3' region MboI cDNA, clone hmd6a12m3.
			D17276	Human HepG2 3' region MboI cDNA, clone hmd6a12m3.

		M27364	Human elongation factor 1 alpha mRNA, 3' end.
		M29548	Human elongation factor 1-alpha (EF1A) mRNA, partial
		L41490	Homo sapiens oncogene P71-1 mRNA, complete cds.
		L41498	Homo sapiens oncogene P71-1 mRNA, complete cds.
		U57846	Human ribosomal protein L39 mRNA, complete cds.
48	CATG TTACCATATC A	-988366	H. sapiens GPx-4 mRNA for phospholipid hydroperoxid
49	CATG GCCTGCTGGG C	-621035	H. sapiens gene for ribosomal protein L38.
50	CATG CCTCGGAATA T	-383489	H. sapiens mRNA for ribosomal protein L6.
51	CATG TACAGAGGGA A	-803369	Human mRNA for DNA-binding protein, TAXREB107, com
		-803369	neoplasm-related C140 product [human, thyroid carc
		-803369	Human beta-tubulin pseudogene.
52	CATG AACGACCTCG T	-24951	Human mRNA fragment encoding beta-tubulin. (from c
		-24951	Human mRNA for neurite outgrowth-promoting protein
53	CATG CCCTGCCTTG T	-358783	Human stimulator of TAR RNA binding (SRB) mRNA, co
54	CATG CCCAGGGAGA A	-346761	Human HepG2 3' region cDNA, clone hmd4f11.
		D16933	H. sapiens mRNA for elongation factor 2.
		-148949	H. sapiens HRPL4 mRNA.
55	CATG AGCACTCCA G	-416261	Human mRNA for ribosomal protein, complete cds.
56	CATG GCCTGGGACA C	D23660	Human 26-kDa cell surface protein TAPA-1 mRNA, com
57	CATG CTAAAAAATA A	-458753	Human glycyl-tRNA synthetase mRNA, complete cds.
58	CATG GGCTGATGTG G	-686319	Human glycyl-tRNA synthetase mRNA, complete cds.
		U09587	Human T-cell mRNA for glycyl tRNA synthetase, comp
		D30658	Human mRNA for HL23 ribosomal protein homologue.
59	CATG ATTCTCAGT A	-253260	Human mRNA for ribosomal protein L17.
		X52839	H. sapiens mRNA for laminin-binding protein.
60	CATG GAAAAATGGT T	-524524	Human mRNA for potential laminin-binding protein (
		X15005	Human 37 kD laminin receptor precursor/p40 ribosom
		U43901	Human colon carcinoma laminin-binding protein mRNA
		J03799	Human laminin receptor (2H5 epitope) mRNA, 5' end.
		M14199	Human mRNA for ribosomal protein L14, complete cds
61	CATG CAGCTCACTG A	-302367	Human (clone CTG-B33) mRNA sequence.
		L10376	CAG-1s1 7 (trinucleotide repeat-containing sequenc
		S80520	Human ribosomal protein S29 mRNA, complete cds.
62	CATG ATAATCTTTT G	-200576	

			L31610	Homo sapiens (clone cori-1cl5) S29 ribosomal prote
63	CATG AATCCTGTGG A	-55227	Z28407	H.sapiens mRNA for ribosomal protein L8.
64	CATG AATAGGTCCA A	-51925	M64716	Human ribosomal protein S25 mRNA, complete cds.
65	CATG AAAAAAAAAA A (C, G,T)	-1	X83412	H.sapiens B1 mRNA for mucin.
			Z32564	H.sapiens FRGAMMA mRNA (819bp) for folate receptor
			Z32633	H.sapiens FRGAMMA' mRNA for folate receptor (817bp
			X76180	H.sapiens mRNA for lung amiloride sensitive Na+ ch
			U08470	Human FR-gamma' mRNA, complete cds.
			U08471	Human folate receptor 3 mRNA, complete cds.
			U48697	Human mariner-like element-containing mRNA, clone
			D28532	Human mRNA for renal Na+-dependent phosphate cotra
			M55914	Human c-myc binding protein (MBP-1) mRNA, complete
			L06175	Homo Sapiens P5-1 mRNA, complete cds.
			S73775	calmitine-mitochondrial calcium-binding protein [h
			S77393	transcript chl38 [human, RF1,RF48 stomach cancer c
			X60036	H.sapiens mRNA for mitochondrial phosphate carrier
66	CATG CCAGAACAGA C	-335945	X79238	H.sapiens mRNA for ribosomal protein L30.
			L16991	Human thymidylate kinase (CDC8) mRNA, complete cds
			X80822	H.sapiens mRNA for ORF.
67	CATG AAGGTGGAGG A	-44683	X52856	Human cyclophilin-related processed pseudogene.
68	CATG CCTAGCTGGA T	-379369	X52857	Human cyclophilin-related processed pseudogene.
			X52854	Human cyclophilin-related processed pseudogene.
			X52851	Human cyclophilin gene for cyclophilin (EC 5.2.1.8
			Y00052	Human mRNA for T-cell cyclophilin.
69	CATG GAACACATCC A	-528694	X63527	H.sapiens mRNA for ribosomal protein L19.
			S56985	ribosomal protein L19 [human, breast cancer cell 1
70	CATG AAGGACATGG G	-41531	X69181	H.sapiens mRNA for ribosomal protein L31.
			X15940	Human mRNA for ribosomal protein L31.
			Z29650	H.sapiens SMCX mRNA.
71	CATG AGGCTACGGA A	-171113	D17233	Human HepG2 3' region MboI cDNA, clone hmd4cl2m3.
72	CATG AGTCCTAGC C	-177610	X08096	Human GST pi gene for glutathione S-transferase pi

			X06547	Human mRNA for class Pi glutathione S-transferase
			X15480	Human mRNA for anionic glutathione-S-transferase (
			X08058	Human glutathione S-transferase pi gene.
			U12472	Human glutathione S-transferase (GST phi) gene, co
			U21689	Human glutathione S-transferase-Plc gene, complete
			U62589	Human glutathione S-transferase Plc (GSTplc) mRNA,
			M69113	Human glutathione S-transferase-III mRNA seq
			M24485	Human fatty acid ethyl ester synthase-III mRNA seq
			X69150	Homo sapiens (clone pHGST-pi) glutathione S-transf
73	CATG TGGTGTGAG G	-965603	M96153	Homo sapiens (clone pHGST-pi) glutathione S-transf
			L06432	Homo sapiens apolipoprotein B gene sequence.
			M17885	Homo sapiens 18S ribosomal protein (HKE3) mRNA seq
74	CATG CTCACATCT C	-475448	M17885	Human acidic ribosomal phosphoprotein P0 mRNA, com
75	CATG GTGTTAACCA G	-769045	L25899	Human ribosomal protein L10 mRNA, complete cds.
76	CATG AGGCTTCCA A	-174037	X58125	Human (D9S55) DNA segment containing (TG)24 repeat
			D17268	Human HepG2 3' region MboI cDNA, clone hmd5h09m3.
			M73791	Human novel gene mRNA, complete cds.
			M64241	Human Wilm's tumor-related protein (QM) mRNA, comp
			S35960	laminin receptor homolog [3' region] (human, mRNA
77	CATG GGATTGGCC T	-671654	M17887	Human acidic ribosomal phosphoprotein P2 mRNA, com
			M11147	Human ferritin L chain mRNA, complete cds.
			M12938	Human ferritin light subunit mRNA, partial cds.
			M10119	Human ferritin light subunit mRNA, complete cds.
78	CATG ATTAACAAAG C	-246019	X04409	Human mRNA for coupling protein G(s) alpha-subunit
			X04408	Human mRNA for coupling protein G(s) alpha subunit
			X56009	Human GSA mRNA for alpha subunit of GsGTP binding
			X07036	Human mRNA stimulatory GTP-binding protein alpha s
			M21142	Human guanine nucleotide-binding protein alpha-sub
			M14631	Human guanine nucleotide-binding protein G-s, alph
79	CATG TGTACCTGTA A	-968173	Z36832	H.sapiens (xs31) mRNA, 835bp.
			K00558	human alpha-tubulin mRNA, complete cds.
80	CATG TGGCCCAACC C	-955718	X56494	H.sapiens M gene for M1-type and M2-type pyruvate
			M23725	Human M2-type pyruvate kinase mRNA, complete cds.
			M26252	Human TCB gene encoding cytosolic thyroid hormone-

81	CATG TAATAAGGT	G	-798764	X67247	H.sapiens rps8 gene for ribosomal protein S8.
82	CATG GCATAATAGG	T	-602315	X89401	H.sapiens mRNA for large subunit of ribosomal prot
				U14967	Human ribosomal protein L21 mRNA, complete cds.
				U25789	Human ribosomal protein L21 mRNA, complete cds.
				L38826	Homo sapiens L21 ribosomal protein gene, partial c
83	CATG TACCATCAAT	A	-807748	X53778	H.sapiens hng mRNA for uracil DNA glycosylase.
				U34995	Human normal keratinocyte subtraction library mRN
				J02642	Human glyceraldehyde 3-phosphate dehydrogenase mRN
				M36164	Human glyceraldehyde-3-phosphate dehydrogenase mRN
				M33197	Human glyceraldehyde-3-phosphate dehydrogenase (CA
84	CATG ATTTGTCCCA	G	-260949	X14957	Human hmgI mRNA for high mobility group protein I.
				X14958	Human hmgI mRNA for high mobility group protein Y.
				M23614	Human HMG-I protein isoform mRNA (HMG1 gene), clon
				M23619	Human HMG-I protein isoform mRNA (HMG1 gene), clon
				L17131	Human high mobility group protein (HMG-I(Y)) gene
				M23615	Human HMG-Y protein isoform mRNA (HMG1 gene), clon
				M23616	Human HMG-Y protein isoform mRNA (HMG1 gene), clon
				M23617	Human HMG-Y protein isoform mRNA (HMG1 gene), clon
				M23618	Human HMG-Y protein isoform mRNA (HMG1 gene), clon
85	CATG GAGGGAGTTT	C	-567488	U14968	Human ribosomal protein L27a mRNA, complete cds.
86	CATG CGCCGCCGGC	T	-416106	U12465	Human ribosomal protein L35 mRNA, complete cds.
87	CATG GTGAACCCCA	ALL	-753749	Z63072	H.sapiens CpG island DNA genomic MseI fragment, cl
88	CATG GTGAACCCCA	ALL	-753749	X16294	Human repetitive DNA containing interspersed repea
89	CATG AAGACAGTGG	C	-33979	X66699	H.sapiens mRNA for ribosomal protein L37a.
				L06499	Homo sapiens ribosomal protein L37a (RPL37A) mRNA,
				L22154	Human ribosomal protein L37a mRNA sequence.
90	CATG CCCCAGCCAG	T	-348755	X55715	Human Hums3 mRNA for 40S ribosomal protein s3.
				U14990	Human XP1PO ribosomal protein S3 (rps3) mRNA, comp
				U14991	Human XP2NE ribosomal protein S3 (rps3) mRNA, comp
				U14992	Human IMR-90 ribosomal protein S3 (rps3) mRNA, com
				S42658	S3 ribosomal protein [human, colon, mRNA, 826 nt].
91	CATG TGGGCAAGC	C	-959498	X63526	H.sapiens mRNA for protein homologous to elongatio
				Z11531	H.sapiens mRNA for elongation factor-1-gamma.

			M55409	Human pancreatic tumor-related protein mRNA, 3' en
92	CATG TGAGGGAATA	A	-928269	Human triosephosphate isomerase mRNA, complete cds
93	CATG GACGACACGA	G	-549145	Human ribosomal protein S28 mRNA, complete cds.
			M58458	Human ribosomal protein S4 (RPS4X) isoform mRNA, c
			M22146	Human scar protein mRNA, complete cds.
94	CATG AACGGGCCA	A	-26261	Homo sapiens macrophage migration inhibitory facto
			M23063	Human glycosylation-inhibiting factor mRNA, comple
			L10612	Homo sapiens macrophage migration inhibitory facto
			M95775	Homo sapiens macrophage migration inhibitory facto
			L19686	Homo sapiens macrophage migration inhibitory facto
			M25639	Human migration inhibitory factor (MIF) mRNA, comp
				Human mRNA for ribosomal protein L32.
95	CATG TGCACGTTTT	C	-935680	Human mRNA from chromosome 15 gene with homology t
			K03002	Human ribosomal protein S27 mRNA, complete cds.
96	CATG CACAACGGT	A	-278636	Human ribosomal protein S27 mRNA, complete cds.
			L19739	Homo sapiens metallopantstimulin (MPS1) mRNA, compl
97	CATG GGAGTGGACA	T	-667269	Homo sapiens ribosomal protein L18 (RPL18) mRNA, c
98	CATG GCCAGGAAG	G	-615043	H.sapiens CpG island DNA genomic MseI fragment, cl
			257572	H.sapiens CpG island DNA genomic MseI fragment, cl
			256073	H.sapiens CpG island DNA genomic MseI fragment, cl
			X53505	Human mRNA for ribosomal protein S12.
99	CATG GGGGAATCG	C	-696375	Human thymosin beta 10 mRNA, complete cds.
			M20259	Human thymosin beta-10 mRNA, complete cds.
100	CATG GCAGCCATCC	G	-599350	Human ribosomal protein L28 mRNA, complete cds.
			D17257	Human HepG2 3' region MboI cDNA, clone hmd5d04m3.
101	CATG TAAGGAGCTG	A	-796831	H.sapiens RPS26 mRNA.
			X69654	H.sapiens mRNA for ribosomal protein S26.
102	CATG GGCAAGCCCC	A	-672342	Human Csa-19 mRNA, complete cds.
			X79239	H.sapiens mRNA for ribosomal protein S13.
			L01124	Human ribosomal protein S13 (RPS13) mRNA, complete
103	CATG GTTCCCTGGC	C	-775658	H.sapiens fau mRNA.
			X65923	H.sapiens pseudogene, trinucleotide repeat regio
			U02523	Human FAU1P pseudogene, trinucleotide repeat regio
104	CATG CCGTCCAAGG	G	-374027	Human ribosomal protein S16 mRNA, complete cds.
	CATG TTGGTCCTCT	G	-1027448	H.sapiens mRNA for homologue to yeast ribosomal pr
			S64030	L41 ribosomal protein homologue (clone 7B6) [human,

105	CATG CAAACCATCC	A	-263478	X12883	Human mRNA for cytokeratin 18.
				X12876	Human mRNA fragment for cytokeratin 18.
				X12881	Human mRNA for cytokeratin 18.
				M24842	Human keratin 18 (K18) gene, complete cds.
				M26325	Human cytokeratin 18 mRNA, 3' end.
				M26326	Human keratin 18 mRNA, complete cds.
				M26327	Human cytokeratin 18 mRNA, 3' end.
				X53777	Human L23 mRNA for putative ribosomal protein.
106	CATG AGCTCTCCCT	G	-161624	D86979	Human male bone marrow myeloblast mRNA for KIAA022
107	CATG AGGTCAGGAG	A(T)	-177315	X55923	Human DNA for Alu element P1N6.
				X79699	H.sapiens ALU repeat, 230bp.
				X12544	Human mRNA for HLA class II DR-beta (HLA-DR B).
				Z77989	H.sapiens flow-sorted chromosome 6 HindIII fragmen
				U11831	Human clone 2102V-I chromosome 18p telomeric seque
				U12580	Human Alu repeat sequence A3.
				U12582	Human Alu repeat sequence B2.
				U12583	Human Alu repeat sequence D1.
				U14694	Human Alu-Sb2 repeat, clone HALUSB08.
				U14695	Human Alu-Sb2 repeat, clone HALUSB15.
				U14696	Human Alu-Sb2 repeat, clone HALUSB27.
				U14697	Human Alu-Sb2 repeat, clone HUM-11.
				U14698	Human Alu-Sb2 repeat, clone HSB-8P.
				U14699	Human Alu-Sb2 repeat, clone HUM-9.
				U14700	Human Alu-Sb2 repeat, clone HALUSB35.
				U14701	Human Alu-Sb2 repeat, clone HSB-2P.
				U14704	Human Alu-Sb2 repeat, clone HUM-3.
				U14706	Human Alu-Sb2 repeat, clone HUM-10.
				U14707	Human Alu-Sb2 repeat, clone HUM-7.
				J00120	Human (Lawn) c-myc proto-oncogene, complete coding
				L34653	Homo sapiens platelet/endothelial cell adhesion mo
				M37521	Human XV2c gene.
				S61789	NF1-neurofibromatosis type 1 (deletion breakpoint,
				S73483	phosphorylase kinase catalytic subunit PHKG2 homol

			S75201	cholinesterase (Alu element) [human, Insertion Mut
			S75337	(Y Alu polymorphism, YAP, polymorphic subfamily-3)
108	CATG GGGCTGGGGT	C	Z49148	H.sapiens mRNA for ribosomal protein L29.
			U10248	Human ribosomal protein L29 (humrpl29) mRNA, compl
			U49083	Human cell surface heparin binding protein HIP mRNA
			D16992	Human cell surface heparin binding protein HIP mRNA
			D16911	Human HepG2 partial cDNA, clone hmd2d02m5.
			J03537	Human HepG2 3' region cDNA, clone hmd3b09.
			M20020	Human ribosomal protein S6 mRNA, complete cds.
				Human ribosomal protein S6 mRNA, complete cds.
109	CATG ACGTTCTCTT	C	-114144	EST
110	CATG TCTCATACC	C	-906438	EST
111	CATG GACTGCGTGC	C	-555450	EST
112	CATG CTTAATCCTG	A	-508767	EST
113	CATG GGTGGCAGG	G	-719435	EST
114	CATG GCCCTCTGCC	A	-613862	EST
115	CATG AACAGAGCA	A	-18469	EST
116	CATG CTGCCGAGCT	C	-497192	EST
117	CATG TTCCTCGGC	A	-1007018	EST
118	CATG AACTAATACT	A	-28872	EST
119	CATG TAGATAATGG	C	-822331	EST
120	CATG GCCACACCCC	A,C	-607318	EST
121	CATG GAACCCCTGG	A	-529899	EST
122	CATG AACTAAAAA	A	-28673	EST
123	CATG GAAATGTAAG	A	-528067	EST
124	CATG ACTCCAAAA	A	-119809	EST
125	CATG GTTCGTGCCA	A	-777109	EST
126	CATG TTACCTCCTT	C	-989024	EST
127	CATG GCACAAGAG	A	-594051	EST
128	CATG CCTGGGTTTC	T	-359102	EST
129	CATG GCTGTATGA	G	-621369	EST
130	CATG CCGTCCGGA	A	-355689	EST
131	CATG AGGAAAGCTG	C	-163999	EST
132	CATG TCAGATCTTT	G	-861056	EST

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133	CATG	CCAGGAGGAA	T	-338081
134	CATG	TCACCCACAC	C	-857362
135	CATG	GTGTTGCACA	A	-769605
136	CATG	GCCGTGTCCG	C	-618199

Isolation of partial cDNA (3' fragment) by 3' directed PCR reaction

This procedure is a modification of the protocol described in Polyak et al. (1997) Nature 389:300. Briefly, the procedure uses SAGE tags in PCR reaction such that the resultant PCR product contains the SAGE tag of interest as well as additional cDNA, the length of which is defined by the position of the tag with respect to the 3' end of the cDNA. The cDNA product derived from such a transcript driven PCR reaction can be used for many applications.

RNA from a source believed to express the cDNA corresponding to a given tag is first converted to double-stranded cDNA using any standard cDNA protocol. Similar conditions used to generate cDNA for SAGE library construction can be employed except that a modified oligo-dT primer is used to drive the first strand synthesis. For example, the oligonucleotide of composition 5'-B-TCC GGC GCG CCG TTT T CC CAG TCA CGA(30)-3', contains a poly-T stretch at the 3' end for hybridization and priming from poly-A tails, an M13 priming site for use in subsequent PCR steps, a 5' Biotin label (B) for capture to streptavidin-coated magnetic beads, and an AscI restriction endonuclease site for releasing the cDNA from the streptavidin-coated magnetic beads. Theoretically, any sufficiently-sized DNA region capable of hybridizing to a PCR primer can be used as well as any other 8 base pair recognizing endonuclease.

cDNA constructed utilizing this or similar modified oligo-dT primer is then processed exactly as described in U.S. Patent No. (insert) up until adapter ligation where only one adapter is ligated to the cDNA pool. After adapter ligation, the cDNA is released from the streptavidin-coated magnetic beads and is then used as a template for cDNA amplification.

Various PCR protocols can be employed using PCR priming sites within the 3' modified oligo-dT primer and the SAGE tag. The SAGE tag-derived PCR primer employed can be of varying length dictated by 5' extension of the tag into the adaptor sequence. cDNA products are now available for a variety of applications.

This technique can be further modified by: (1) altering the length and/or content of the modified oligo-dT primer; (2) ligating adaptors other than that previously employed within the SAGE protocol; (3) performing PCR from template retained on the streptavidin-coated magnetic beads; and (4) priming first strand cDNA synthesis with non-oligo-dT based primers.

Isolation of cDNA using GeneTrapper or modified GeneTrapper Technology

The reagents and manufacturer's instructions for this technology are commercially available from Life Technologies, Inc., Gaithersburg, Maryland. Briefly, a complex population of single-stranded phagemid DNA containing directional cDNA inserts is enriched for the target sequence by hybridization in solution to a biotinylated oligonucleotide probe complementary to the target sequence. The hybrids are captured on streptavidin-coated paramagnetic beads. A magnet retrieves the paramagnetic beads from the solution, leaving nonhybridized single-stranded DNAs behind. Subsequently, the captured single-stranded DNA target is released from the biotinylated oligonucleotide. After release, the cDNA clone is further enriched by using a nonbiotinylated target oligonucleotide to specifically prime conversion of the single-stranded target to double-stranded DNA. Following transformation and plating, typically 20% to 100% of the colonies represent the cDNA clone of interest. To identify the desired cDNA clone, the colonies may be screened by colony hybridization using the ³²P-labeled oligonucleotide as described above for solution hybridization, or alternatively by DNA sequencing and alignment of all sequences obtained from numerous clones to determine a consensus sequence.

The genes which are identified herein as being differentially expressed in normal and cancer cells can be used diagnostically and prognostically. Transcription levels in a test sample suspected of being neoplastic can be determined and compared to the levels in normal colon cells. The test sample may be from any tissue suspected of neoplasia, and particularly from either suspected colorectal or suspected pancreatic cancer cells. The control cells for

the purposes of comparison are normal cells, preferably of the same tissue type as the test sample, e.g., colon cells, or pancreatic duct epithelial cells. Upregulation of transcription or downregulation of transcription is therefore diagnostic of the neoplastic state, depending on what gene is used as a test reagent. Similarly, transcription levels can be monitored to assess patient responses to anti-tumor therapies. Transcription levels will also provide prognostic information. For example, the level of transcription in a test sample can be compared to levels found in *bona fide* normal and tumor cells. More extreme deviations from normal expression levels indicate a poorer prognosis.

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Transcription levels can be determined according to any means known in the art. These include, without limitation, Northern blots, nuclear run-on assays, *in vitro* transcription assays, primer extension assays, quantitative reverse transcriptase-polymerase chain reactions (RT-PCR), and hybrid filter binding assays. These techniques are well known in the art. See J.C. Alwine, D.J. Kemp, G.R. Stark, *Proc. Natl. Acad. Sci. U.S.A.* 74, 5350 (1977); K. Zinn, D. Di-Maio, T. Maniatis, *Cell* 34, 865 (1983); G. Veres, R.A. Gibbs, S.E. Scherer, C.T. Caskey, *Science* 237, 415 (1987).

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Similarly, upregulated genes and downregulated genes can be detected by measuring expression of their protein products. This can be done by any means known in the art, including but not limited to Western (immuno) blot, enzyme linked immunoadsorbent assay, radioimmunoassay, and enzyme assay. Such techniques are well known in the art. Protein products can be detected in tissue samples of a test patient, using a suspect sample as a test sample, and a matched normal tissue sample from the same tissue type as a control. If normal tissue is not available then a closely related tissue type can be used. Desirably both the samples being compared will be from the same individual. Alternatively, aberrant expression levels of protein products can be detected in body samples, such as blood, serum, feces, urine, sputum. As a control, a normal matched sample can be used from a healthy individual. Aberrant expression levels of transcripts can also be detected in such body samples, particularly in blood and serum.

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Probes for use in the assays for transcription levels of particular genes or sets of genes may be RNA or DNA. The probes will be isolated substantially free of other cellular RNAs or DNAs. If the reagent contains one probe then it will comprise at least 50% of the nucleic acids in the reagent composition. If the reagent contains more than one probe, then the proportion will decrease accordingly, so that specific probes will still comprise at least 50% of the nucleic acids in the reagent composition.

Probes can be labeled according to any means known in the art. These may include radioactive labels, fluorescent labels, enzymatic labels, and binding partner labels such as biotin. Means for labeling and detecting probes are well known in the art. Probes comprise at least 10, 11, 12, 15, 20, or 30 contiguous nucleotides of a selected gene.

This invention provides proteins or polypeptides expressed from the polynucleotides of this invention, which is intended to include wild-type and recombinantly produced polypeptides and proteins from procaryotic and eucaryotic host cells, as well as muteins, analogs and fragments thereof. In some embodiments, the term also includes antibodies and anti-idiotypic antibodies.

It is understood that functional equivalents or variants of the wild-type polypeptide or protein also are within the scope of this invention, for example, those having conservative amino acid substitutions. Other analogs include fusion proteins comprising a protein or polypeptide.

The proteins and polypeptides of this invention are obtainable by a number of processes well known to those of skill in the art, which include purification, chemical synthesis and recombinant methods. Full length proteins can be purified from a colon or pancreatic cell or tissue lysate by methods such as immunoprecipitation with antibody, and standard techniques such as gel filtration, ion-exchange, reversed-phase, and affinity chromatography using a fusion protein as shown herein. For such methodology, see for example Deutscher et al. (1999) Guide To Protein Purification: Methods In Enzymology (Vol. 182, Academic Press). Accordingly, this invention also

provides the processes for obtaining these proteins and polypeptides as well as the products obtainable and obtained by these processes.

The proteins and polypeptides also can be obtained by chemical synthesis using a commercially available automated peptide synthesizer such as those manufactured by Perkin Elmer/Applied Biosystems, Inc., Model 430A or 431A, Foster City. The synthesized protein or polypeptide can be precipitated and further purified, for example by high performance liquid chromatography (HPLC). Accordingly, this invention also provides a process for chemically synthesizing the proteins of this invention by providing the sequence of the protein and reagents, such as amino acids and enzymes and linking together the amino acids in the proper orientation and linear sequence.

Alternatively, the proteins and polypeptides can be obtained by well-known recombinant methods as described, for example, in Sambrook et al., (1989), *supra*, using the host cell and vector systems described above.

Also provided by this application are the polypeptides and proteins described herein conjugated to a detectable agent for use in the diagnostic methods. For example, detectably labeled proteins and polypeptides can be bound to a column and used for the detection and purification of antibodies. They also are useful as immunogens for the production of antibodies as described below. The proteins and fragments of this invention are useful in an in vitro assay system to screen for agents or drugs, which modulate cellular processes.

The proteins of this invention also can be combined with various liquid phase carriers, such as sterile or aqueous solutions, pharmaceutically acceptable carriers, suspensions and emulsions. Examples of non-aqueous solvents include propyl ethylene glycol, polyethylene glycol and vegetable oils. When used to prepare antibodies, the carriers also can include an adjuvant that is useful to non-specifically augment a specific immune response. A skilled artisan can easily determine whether an adjuvant is required and select one. However, for the purpose of illustration only, suitable adjuvants include, but

are not limited to Freund's Complete and Incomplete, mineral salts and polynucleotides.

5 This invention also provides a pharmaceutical composition comprising any of a protein, analog, mutein, polypeptide fragment, antibody, antibody fragment or anti-idiotypic antibody of this invention, alone or in combination with each other or other agents, and an acceptable carrier. These compositions are useful for various diagnostic and therapeutic methods.

10 Antibodies can be generated using the proteins encoded by the transcripts identified by the tags disclosed herein. Use of all or portions of the protein as immunogens is routine in the art. Similarly, fusion proteins can be used as immunogens. Antibodies can be affinity purified using the proteins or portions thereof used as immunogens. Similarly, monoclonal antibodies specifically immunoreactive with the protein sequences of the invention can be generated according to techniques which are well known in the art.

15 Antibodies can be used analytically to quantitate the expression of particular transcripts identified herein as upregulated or downregulated in cancer. In addition, antibodies can be conjugated or non-covalently linked to cytotoxic agents, such as cytotoxins, radionuclides, chemotherapeutic drugs, etc. Such antibodies can be used therapeutically to specifically target cancer cells in which the protein antigens are upregulated. These include the proteins encoded by the transcripts identified by the tags shown in Tables 2, 4, and 5. Means of making such linked cytotoxic antibodies and of administering the same are well known in the art.

25 Also provided by this invention is an antibody capable of specifically forming a complex with the proteins or polypeptides as described above. The term "antibody" includes polyclonal antibodies and monoclonal antibodies. The antibodies include, but are not limited to mouse, rat, and rabbit or human antibodies.

30 Laboratory methods for producing polyclonal antibodies and monoclonal antibodies, as well as deducing their corresponding nucleic acid sequences, are known in the art, see Harlow and Lane (1988) supra and

5 Sambrook et al. (1989) supra. The monoclonal antibodies of this invention can be biologically produced by introducing protein or a fragment thereof into an animal, e.g., a mouse or a rabbit. The antibody producing cells in the animal are isolated and fused with myeloma cells or heteromyeloma cells to produce hybrid cells or hybridomas. Accordingly, the hybridoma cells producing the monoclonal antibodies of this invention also are provided.

10 Thus, using the protein or fragment thereof, and well known methods, one of skill in the art can produce and screen the hybridoma cells and antibodies of this invention for antibodies having the ability to bind the proteins or polypeptides.

15 If a monoclonal antibody being tested binds with the protein or polypeptide, then the antibody being tested and the antibodies provided by the hybridomas of this invention are equivalent. It also is possible to determine without undue experimentation, whether an antibody has the same specificity as the monoclonal antibody of this invention by determining whether the antibody being tested prevents a monoclonal antibody of this invention from binding the protein or polypeptide with which the monoclonal antibody is normally reactive. If the antibody being tested competes with the monoclonal antibody of the invention as shown by a decrease in binding by the monoclonal antibody of this invention, then it is likely that the two antibodies bind to the same or a closely related epitope. Alternatively, one can pre-incubate the monoclonal antibody of this invention with a protein with which it is normally reactive, and determine if the monoclonal antibody being tested is inhibited in its ability to bind the antigen. If the monoclonal antibody being tested is inhibited then, in all likelihood, it has the same, or a closely related, epitopic specificity as the monoclonal antibody of this invention.

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30 The term "antibody" also is intended to include antibodies of all isotypes. Particular isotypes of a monoclonal antibody can be prepared either directly by selecting from the initial fusion, or prepared secondarily, from a parental hybridoma secreting a monoclonal antibody of different isotype by using the sib selection technique to isolate class switch variants using the

procedure described in Steplewski et al. (1985) Proc. Natl. Acad. Sci. 82:8653 or Spira et al. (1984) J. Immunol. Methods 74:307.

This invention also provides biological active fragments of the polyclonal and monoclonal antibodies described above. These "antibody fragments" retain some ability to selectively bind with its antigen or immunogen. Such antibody fragments can include, but are not limited to:

- (1) Fab,
- (2) Fab',
- (3) F(ab')₂,
- (4) Fv, and
- (5) SCA

A specific example of "a biologically active antibody fragment" is a CDR region of the antibody. Methods of making these fragments are known in the art, see for example, Harlow and Lane, (1988) supra.

The antibodies of this invention also can be modified to create chimeric antibodies and humanized antibodies (Oi, et al. (1986) BioTechniques 4(3):214). Chimeric antibodies are those in which the various domains of the antibodies' heavy and light chains are coded for by DNA from more than one species.

The isolation of other hybridomas secreting monoclonal antibodies with the specificity of the monoclonal antibodies of the invention can also be accomplished by one of ordinary skill in the art by producing anti-idiotypic antibodies (Herlyn, et al. (1986) Science 232:100). An anti-idiotypic antibody is an antibody which recognizes unique determinants present on the monoclonal antibody produced by the hybridoma of interest.

Idiotypic identity between monoclonal antibodies of two hybridomas demonstrates that the two monoclonal antibodies are the same with respect to their recognition of the same epitopic determinant. Thus, by using antibodies to the epitopic determinants on a monoclonal antibody it is possible to identify other hybridomas expressing monoclonal antibodies of the same epitopic specificity.

5 It is also possible to use the anti-idiotypic technology to produce monoclonal antibodies which mimic an epitope. For example, an anti-idiotypic monoclonal antibody made to a first monoclonal antibody will have a binding domain in the hypervariable region which is the mirror image of the epitope bound by the first monoclonal antibody. Thus, in this instance, the anti-idiotypic monoclonal antibody could be used for immunization for production of these antibodies.

10 As used in this invention, the term "epitope" is meant to include any determinant having specific affinity for the monoclonal antibodies of the invention. Epitopic determinants usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains and usually have specific three dimensional structural characteristics, as well as specific charge characteristics.

15 The antibodies of this invention can be linked to a detectable agent or label. There are many different labels and methods of labeling known to those of ordinary skill in the art.

20 The antibody-label complex is useful to detect the protein or fragments in a sample, using standard immunochemical techniques such as immunohistochemistry as described by Harlow and Lane (1988) supra. Competitive and non-competitive immunoassays in either a direct or indirect format are examples of such assays, e.g., enzyme linked immunoassay (ELISA) radioimmunoassay (RIA) and the sandwich (immunometric) assay. Those of skill in the art will know, or can readily discern, other immunoassay formats without undue experimentation.

25 The coupling of antibodies to low molecular weight haptens can increase the sensitivity of the assay. The haptens can then be specifically detected by means of a second reaction. For example, it is common to use haptens such as biotin, which reacts avidin, or dinitrophenyl, pyridoxal, and fluorescein, which can react with specific anti-hapten antibodies. See Harlow and Lane (1988) supra.

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The monoclonal antibodies of the invention also can be bound to many different carriers. Thus, this invention also provides compositions containing the antibodies and another substance, active or inert. Examples of well-known carriers include glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylases, natural and modified celluloses, polyacrylamides, agaroses and magnetite. The nature of the carrier can be either soluble or insoluble for purposes of the invention. Those skilled in the art will know of other suitable carriers for binding monoclonal antibodies, or will be able to ascertain such, using routine experimentation.

Compositions containing the antibodies, fragments thereof or cell lines which produce the antibodies, are encompassed by this invention. When these compositions are to be used pharmaceutically, they are combined with a pharmaceutically acceptable carrier.

The present invention also provides a screen for various agents which modulate the expression of a gene in a pancreatic or colon cell. To practice the method *in vitro*, suitable cell cultures or tissue cultures are first provided. The cell can be a cultured cell or a genetically modified cell in which a transcript from SEQ ID NOS:1-732, or their complements, is expressed. Alternatively, the cells can be from a tissue biopsy. The cells are cultured under conditions (temperature, growth or culture medium and gas (CO₂)) and for an appropriate amount of time to attain exponential proliferation without density dependent constraints. It also is desirable to maintain an additional separate cell culture; one which does not receive the agent being tested as a control.

As is apparent to one of skill in the art, suitable cells may be cultured in microtiter plates and several agents may be assayed at the same time by noting genotypic changes, phenotypic changes or cell death.

When the agent is a composition other than a DNA or RNA, the agent may be directly added to the cell culture or added to culture medium for addition. As is apparent to those skilled in the art, an "effective" amount must be added which can be empirically determined. When the agent is a polynucleotide, it may be directly added by use of a gene gun or

electroporation. Alternatively, it may be inserted into the cell using a gene delivery vehicle or vector as described above.

An agent is a potential therapeutic if it alters the expression of gene in the cell. Altered expression can be detected by assaying for altered mRNA expression or protein expression using the probes, primers and antibodies as described herein.

For the purposes of this invention, an "agent" is intended to include, but not be limited to a biological or chemical compound such as a simple or complex organic or inorganic molecule, a peptide, a protein (e.g. antibody) or a polynucleotide (e.g. anti-sense). A vast array of compounds can be synthesized, for example polymers, such as polypeptides and polynucleotides, and synthetic organic compounds based on various core structures, and these are also included in the term "agent". In addition, various natural sources can provide compounds for screening, such as plant or animal extracts, and the like. It should be understood, although not always explicitly stated that the agent is used alone or in combination with another agent, having the same or different biological activity as the agents identified by the inventive screen. The agents and methods also are intended to be combined with other therapies.

The above disclosure generally describes the present invention. A more complete understanding can be obtained by reference to the following specific examples which are provided herein for purposes of illustration only, and are not intended to limit the scope of the invention.

EXAMPLE 1

This example demonstrates the characterization of the general transcription of human colorectal epithelium, colorectal cancers, and pancreatic cancers.

We used the recently developed SAGE (serial analysis of gene expression) method to identify and quantify a total of 303,706 transcripts derived from human colorectal (CR) epithelium, CR cancers or pancreatic cancers (Table 1A) (3). These transcripts represented approximately 48,741

different genes (4) that ranged in average expression from 1 copy per cell to as many as 5,300 copies per cell (5). The number of different transcripts observed in each cell population varied from 14,247 to 20,471. The bulk of the mRNA mass (75%) consisted of transcripts expressed at more than five copies per cell on average (Table 1B). In contrast, the majority (86%) of transcripts were expressed at less than 5 copies per cell, but in aggregate this low abundance class represented only 25% of the mRNA mass. This distribution was consistently observed among the different samples analyzed and was consistent with previous studies of RNA abundance classes based on RNA-DNA reassociation kinetics (Rot curves). Monte Carlo simulations revealed that our analyses had a 92% probability of detecting a transcript expressed at an average of three copies per cell (7).

Table 1 - Summary of SAGE Analysis

A. Overall Summary

	Normal		Colon		Colon		Pancreatic		Total
	Colon	Tumors	Tumors	Cell Lines	Cell Lines	Tumors	Cell Lines		
Total Tags	62,168	60,878	60,878	60,373	61,592	58,695	303,706		
Unique Genes ¹	14,721	19,690	17,092	20,471	14,247	48,741			
GenBank ²	8,753 (59)	10,490 (53)	10,193 (60)	11,547 (56)	8,922 (63)	26,339 (54)			

¹ Indicates the number of different genes represented by the total tags analyzed (4).

² Indicates the number of genes that matched an entry in GenBank. The number in parentheses indicates the corresponding percentage of total unique tags.

Table 1 - Summary of SAGE Analysis

B. Summarized by Abundance Classes*

Copies/Cell	Normal		Colon		Colon		Pancreatic		Pancreatic Cell	
	Colon		Tumors		Cell Lines		Tumors		Lines	Total
> 500										
Unique Genes	62 (29)		54 (25)		54 (19)		32 (11)		70 (26)	55 (19)
GenBank	59 (95)		52 (96)		53 (98)		32 (100)		70 (100)	54 (98)
> 50 and ≤ 500										
Unique Genes	645 (28)		470 (21)		618 (27)		657 (29)		585 (27)	595 (26)
GenBank	545 (84)		429 (91)		579 (94)		609 (93)		529 (90)	553 (93)
> 5 and ≤ 50										
Unique Genes	4,569 (27)		5,011 (29)		5,733 (34)		6,146 (36)		4,895 (31)	6,209 (30)
GenBank	2,893 (63)		3,204 (64)		3,682 (64)		4,054 (66)		3,168 (65)	4,241 (68)

≤ 5						
Unique Genes	9,445 (16)	14,155 (25)	10,687 (20)	13,636 (24)	8,697 (16)	41,882 (25)
GenBank	5,256 (56)	6,805 (48)	5,879 (55)	6,852 (50)	5,155 (59)	21,491 (51)

*For unique genes, the first number denotes the number of different genes (4) represented in the indicated abundance class. The number in parentheses indicates the mass fraction (X100) of total transcripts represented by the indicated abundance class. For GenBank entries, the first number indicates the number of different genes that matched an entry in GenBank in the indicated abundance class. The number in parentheses indicates the corresponding percentage of total genes.

Many of the SAGE tags appeared to represent previously undescribed transcripts, as only 54% of the tags matched entries in GenBank (Table 1). Twenty percent of these matching transcripts corresponded to characterized mRNA sequence entries in GenBank, whereas 80% matched uncharacterized EST entries. As expected, the likelihood of a tag being present in the databases was related to abundance; GenBank matches were identified for 98% of the transcripts expressed at more than 500 copies per cell but for only 51% of the transcripts expressed at ≤ 5 copies per cell. Because the SAGE data provide a quantitative assay of transcript abundance, unaffected by differences in cloning or PCR efficiency, these data provide an independent and relatively unbiased estimate of the current completeness of publicly available EST databases.

EXAMPLE 2

This example demonstrates a comparison of the expression pattern of normal colon epithelium and primary colon cancers.

Comparison of expression patterns between normal colon epithelium and primary colon cancers revealed that the majority of transcripts were expressed at similar levels (Fig. 1A). However, the expression profiles also revealed 289 transcripts that were expressed at significantly different levels [$P < 0.01$, (8)]. Of these 289, 181 were decreased in colon tumors compared to normal colon (average decrease 10-fold; Fig. 1B; examples in Fig. 2A). Conversely, 108 transcripts were expressed at higher levels in the colon cancers than in normal colon (average increase 13-fold; Fig. 1C; examples in Fig. 2A). Monte Carlo simulations indicated that the analysis would have detected over 95% of those transcripts expressed at a 6-fold or greater level in normal vs. tumor cells or vice versa (9). Because relatively stringent criteria were used for defining differences [$P < 0.01$, (8)], the number of differences reported above is likely to be an underestimate.

EXAMPLE 3

This example demonstrates the similarities and differences between cancer cell line transcription and transcription of primary cancer tissues.

To determine how many of the 289 differences were independent of the cellular microenvironment of cancers *in vivo*, SAGE data from CR cancer cell lines was compared to that from primary CR cancer tissues (Fig. 1B, 1C). Perhaps surprisingly, the majority of transcripts (130 of 181) that were expressed at reduced levels in cancer cells *in vivo* were also expressed at significantly lower levels in the cell lines (Fig. 1B). Likewise, a significant fraction of the transcripts expressed at increased levels in primary cancers were also expressed at higher levels in the CR cancer cell lines (Fig. 1C). Thus, many of the gene expression differences that distinguish normal from tumor cells *in vivo* persist during *in vitro* growth. However, despite these similarities there were also many differences. For example, only 47 of 228 genes expressed at higher levels in CR cancer cell lines were also expressed at high levels in the primary CR cancers.

In combination, comparing the expression pattern of CR cancer cells (in *vivo* or *in vitro*) to normal colon revealed 548 differentially expressed transcripts (Fig. 1B,C, Tables 2 and 3). The average difference in expression for these transcripts was 15 fold. Although the ability to detect differences is influenced by the magnitude of the variance with the power to detect smaller differences being less, 92 transcripts that were less than three fold different were identified among the 548 transcripts. However, those genes exhibiting the greatest differences in expression are likely to be the most biologically important.

EXAMPLE 4

This example demonstrates the similarities and differences between colorectal cancer transcription and pancreatic cancer transcription.

To determine whether the changes noted in CR cancers were neoplasia or cell type specific, we performed SAGE on mRNA derived from pancreatic cancers. A total of 404 transcripts were expressed at higher levels in pancreatic cancers compared to normal colon epithelium (examples in Fig. 2B). The majority (268) of these transcripts were pancreas-specific (10) (Example in Fig. 2C) although 136 were also expressed at high levels in CR cancers. These 136 transcripts constituted 47% of the 289 transcripts increased in CR cancers relative to normal colon and are likely to be related to the neoplastic process rather than to the specific cell type of origin.

EXAMPLE 5

This example demonstrates the reproducibility of the transcription patterns observed among a larger number of cancer samples.

One question that arose from these data is the potential heterogeneity of expression between individual tumors. The SAGE data were acquired from two examples of each tissue type (normal colon, primary CR cancer, CR cancer cell line, etc.). To examine the generality of these expression profiles, we arbitrarily selected 27 differentially expressed transcripts and evaluated them in six to twelve samples of normal colon and primary cancers by Northern blot analysis (11). In general, expression patterns were very reproducible among different samples. Of 10 genes with elevated expression in normal colon relative to CR cancers as determined by SAGE, each was detected in the normal colon samples and was expressed at considerably lower levels in tumors (examples in Fig. 2A). Similarly, most of the genes identified by SAGE as increased in CR or pancreatic cancers were confirmed to be reproducibly expressed in the majority of primary cancers examined by Northern blot (examples in Fig. 2A). It is important to note, however, that there were differences among the cancers, with a few cancers exhibiting particularly high or low levels of individual transcripts. Such differences in gene expression

undoubtedly contribute to the observed heterogeneity in biological properties of cancers derived from the same organ .

EXAMPLE 6

5 This example demonstrates the identities of some of the transcripts which were found to be differentially expressed in tumor and normal tissues. What are the identities of the differentially expressed genes? Of the 548 differentially expressed transcripts, 337 were tentatively identified through database comparisons. When tested, the great majority (93%) of these identifications proved to be legitimate (13), as expected from previous SAGE
10 analyses . Although a large number of differentially expressed genes were identified, some simple patterns did emerge. For example, genes that were expressed at higher levels in normal colon epithelium than in CR tumors were often differentiation-related. These genes included liver fatty acid binding protein , cytokeratin 20 , carbonic anhydrase , guanylin and uroguanylin ,
15 which are known to be important for the normal physiology or architecture of the colon epithelium (Table 2). On the other hand, genes that were increased in CR cancers were often related to the robust growth characteristics that these cells exhibit. For example, gene products associated with protein synthesis, including 48 ribosomal proteins, five elongation factors, and five genes
20 involved in glycolysis were observed to be elevated in both CR and pancreatic cancers compared to normal colon cells. Although the majority of the transcripts could not have been predicted to be differentially expressed in cancers, several have previously been shown to be dysregulated in neoplastic cells. The latter included IGFII , B23 nucleophosmin, the Pi form of
25 glutathione S-transferase, and several ribosomal proteins which were all increased in cancer cells as previously reported. Likewise, Dra and gelsolin were both decreased in cancer as previously reported. Surprisingly, two widely studied oncogenes, *c-fos* and *c-erbB3*, were expressed at much higher levels in normal colon epithelium than CR cancers, in contrast to their up-regulation in
30 transformed cells .

In summary, these data provide basic information necessary for understanding the gene expression differences that underlie cancer phenotypes. They additionally provide a necessary framework for interpreting the significance of individual differentially expressed genes. Although this study demonstrated that a large number of such differences exist (approximately 500 at the depth of analysis employed), it was equally remarkable that the fraction of transcripts exhibiting significant differences was relatively small, representing 1.5 % of the transcripts detected in any given cell type (26). The fact that many, but not all, of the differences were preserved during in vitro culture demonstrates the utility of cultured lines for examination of some aspects of gene expression, but also provides a note of caution in relying on such lines to perfectly mimic tumors in their natural environment. Finally, the finding that hundreds of specific genes are expressed at different levels in CR cancers, and that some of these are also expressed differentially in pancreatic cancers, provides a wealth of new reagents for future biologic and diagnostic experimentation.

REFERENCES AND NOTES

1. M. D. Adams, *et al.*, *Nature* **377**, **supp. 28**, 3 (1995); M. Schena, D. Shalon, R. W. Davis, P. O. Brown, *Science* **270**, 467 (1995); J. Derisi, *et al.*, *Nature Genetics* **14**, 457 (1996); T. M. Gress, *et al.*, *Oncogene* **13**, 1819 (1996); D. J. Lockhart, *et al.*, *Nature Biotechnology* **14**, 1675 (1996); M. Schena, *et al.*, *Proc Natl Acad Sci U S A* **93**, 10614 (1996).
2. V. E. Velculescu, L. Zhang, B. Vogelstein, K. W. Kinzler, *Science* **270**, 484 (1995); V. E. Velculescu, *et al.*, *Cell* **88**, 243 (1997).
3. To minimize individual variation, approximately equal numbers of tags (30,000) were derived from two different patients for each tissue. For primary tumors (two CR carcinomas and two pancreatic adenocarcinomas), RNA was isolated from portions of tumors judged to contain 60%-90% tumor cells by histopathology. The cells grown in vitro were derived from CR (SW837, Caco2) and pancreatic (ASPC-1, PL45) cancer cell lines. CR epithelial cells were isolated from sections of normal colon mucosa from two patients using EDTA as previously described [S. Nakamura, I. Kino, S. Baba, *Gut* **34**, 1240 (1993)]. Histopathology confirmed that the isolated cells were greater than 90% epithelial. Isolation of Poly-A RNA and SAGE was performed as previously described (2). SAGE data was analyzed by means of SAGE software and GenBank Release 95 as previously described (2).
4. A total of 69,393 different SAGE tags were identified among the 303,706 tags analyzed. A small fraction of these different tags were likely due to sequencing errors. SAGE analysis of yeast (2), wherein the entire genomic sequence is known, demonstrated a sequencing error rate of ~ 0.7%, translating to a SAGE tag error rate of 6.8% ($1 - 0.993^{10}$). Because these sequencing mistakes are essentially random, they do not substantially affect the analysis although they could artificially inflate the number of unique genes identified. Therefore, to be conservative, we reduced our estimate of unique genes identified by this maximum tag error rate (e.g., 6.8% of 303,706 total tags). The number of different tags derived from the same gene due to alternative splicing was assumed to be negligible.

5. Abundances can be simply determined by dividing the observed number of tags for a given transcript by the total number of tags obtained. An estimate of approximately 300,000 transcripts per cell was used to convert the abundances to copies per cell [N. D. Hastie, J. O. Bishop, *Cell* 9, 761 (1976)].

5 6. J. O. Bishop, J. G. Morton, M. Rosbash, M. Richardson, *Nature* 250, 199 (1974); B. Lewin, *Gene Expression Vol 2* (John Wiley and sons, New York 1980).

7. Computer simulations indicated that analysis of 300,000 tags would yield a 92 % chance of detecting a tag for a transcript whose expression was at least three copies per cell on average among the tissues examined and assuming 300,000 transcripts per cell.

8. To minimize the number of assumptions and to account for the large number of comparisons being made, Monte Carlo analysis was used for determining statistical significance. The null hypothesis was that the level, kind, and distribution of transcripts were the same for cancer and normal cells. For each transcript, 100,000 simulations were performed to determine the relative likelihood due to chance alone ("p-chance") of obtaining a difference in expression equal to or greater than the observed difference, given the null hypothesis. This likelihood was converted to an absolute probability value by simulating 40 experiments in which a representative number of transcripts (27,993 transcripts in each experiment) was identified and compared. The distribution of transcripts used for these simulations was derived from the average level of expression observed in the original samples. The distribution of the p-chance scores obtained in the 40 simulated experiments (false positives) was then compared to those obtained experimentally. Based on this comparison, a maximum value of 0.0005 was chosen for p-chance. This yielded a false positive rate that was no higher than 0.01 for the least significant p-chance value below the cutoff.

9. Two hundred simulations assuming an abundance of 0.0001 in one sample and 0.0006 in a second sample revealed a significant difference ($P < 0.01$, [8]) 95% of the time.

10. It is not possible to obtain pancreatic ductal epithelium, from which pancreatic carcinomas arise, in sufficient quantities to perform SAGE. It is therefore not possible to determine whether these transcripts were derived from genes that were highly expressed only in pancreatic cancers or were also expressed in pancreatic duct cells.
11. Total RNA isolation and Northern blot analysis was performed as described [W. S. el-Deiry, *et al.*, *Cell* **75**, 817 (1993)].
12. A. H. Owens, D. S. Coffey, S. B. Baylin, Eds., *Tumor Cell Heterogeneity: Origins and Implications* (Academic Press, New York, 1982).
13. Northern blot analyses were done on 45 of the 337 differentially expressed transcripts with tentative database matches. In three cases, the pattern of expression was not differentially expressed as predicted by SAGE and, for the purposes of this calculation, were presumed to represent incorrect database matches.
14. D. C. Rubin, D. E. Ong, J. I. Gordon, *Proc Natl Acad Sci U S A* **86**, 1278 (1989); K. Okubo, J. Yoshii, H. Yokouchi, M. Kameyama, K. Matsubara, *DNA Res* **1**, 37 (1994).
15. R. Moll, *et al.*, *Differentiation* **53**, 75 (1993).
16. J. Sowden, S. Leigh, I. Talbot, J. Delhanty, Y. Edwards, *Differentiation* **53**, 67 (1993).
17. F. J. de Sauvage, *et al.*, *Proc Natl Acad Sci U S A* **89**, 9089 (1992).
18. R. C. Wiegand, *et al.*, *FEBS Lett* **311**, 150 (1992).
19. J. V. Tricoli, *et al.*, *Cancer Res* **46**, 6169 (1986); S. Lambert, J. Vivario, J. Boniver, R. Gol-Winkler, *Int J Cancer* **46**, 405 (1990).
20. W. Y. Chan, *et al.*, *Biochemistry* **28**, 1033 (1989).
21. J. D. Hayes, D. J. Pulford, *Crit Rev Biochem Mol Biol* **30**, 445 (1995).
22. G. F. Barnard, *et al.*, *Cancer Res* **52**, 3067 (1992); P. J. Chiao, D. M. Shin, P. G. Sacks, W. K. Hong, M. A. Tainsky, *Mol Carcinog* **5**, 219 (1992); N. Kondoh, C. W. Schweinfest, K. W. Henderson, T. S. Papas,

Cancer Res **52**, 791 (1992); G. F. Barnard, *et al.*, *Cancer Res* **53**, 4048 (1993); M. G. Denis, *et al.*, *Int J Cancer* **55**, 275 (1993); J. M. Frigerio, *et al.*, *Hum Mol Genet* **4**, 37 (1995).

5 23. C. W. Schweinfest, K. W. Henderson, S. Suster, N. Kondoh, T. S. Papas, *Proc Natl Acad Sci U S A* **90**, 4166 (1993).

 24. M. Tanaka, *et al.*, *Cancer Res* **55**, 3228 (1995); D. Medina, F. S. Kittrell, C. J. Oborn, M. Schwartz, *Cancer Res* **53**, 668 (1993).

 25. A. D. Miller, T. Curran, I. M. Verma, *Cell* **36**, 51 (1984); M. H. Kraus, W. Issing, T. Miki, N. C. Popescu, S. A. Aaronson, *Proc Natl Acad Sci U S A* **86**, 9193 (1989).
10

 26. In the case of normal and neoplastic colon cancer tissue, 548 differentially transcripts were identified among the 36,125 unique transcripts.

 27. All references cited are hereby incorporated by reference herein.

 28. Sequences tags in Tables 2-4 are consecutively numbered to
15 form SEQ ID NOS: 1-732.

CLAIMS

1. A method of diagnosing colon cancer in a sample suspected of being neoplastic, comprising the steps of:

5 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 3;

10 identifying the first sample as neoplastic when the level of the at least one transcript is found to be lower in the first sample than in the second sample.

2. A method of diagnosing colon cancer in a sample suspected of being neoplastic, comprising the steps of:

15 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 2;

20 identifying the first sample as neoplastic when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

3. The method of claim 1 wherein a comparison of at least two of said transcripts is performed.

25 4. The method of claim 2 wherein a comparison of at least two of said transcripts is performed.

5. The method of claim 1 wherein a comparison of at least five of said transcripts is performed.
6. The method of claim 2 wherein a comparison of at least five of said transcripts is performed.
- 5 7. The method of claim 1 wherein a comparison of at least ten of said transcripts is performed.
8. The method of claim 2 wherein a comparison of at least ten of said transcripts is performed.
- 10 9. The method of claim 1 wherein a comparison of at least twenty of said transcripts is performed.
10. The method of claim 2 wherein a comparison of at least twenty of said transcripts is performed.
11. The method of claim 1 wherein a comparison of at least thirty of said transcripts is performed.
- 15 12. The method of claim 2 wherein a comparison of at least thirty of said transcripts is performed.
13. An isolated and purified human nucleic acid molecule which comprises a SAGE tag selected from SEQ ID NO:1-732.
14. The nucleic acid molecule of claim 13 which is a cDNA molecule.

15. The nucleic acid molecule of claim 13 wherein the SAGE tag is located at the 3' end of the molecule, adjacent to the 3'-most NlaIII restriction enzyme site.
- 5 16. An isolated nucleotide probe comprising at least 10 nucleotides of a human nucleic acid molecule, wherein the human nucleic acid molecule comprises a SAGE tag selected from SEQ ID NO: 1-732.
17. The probe of claim 16 which comprises the selected SAGE tag.
18. A diagnostic reagent for evaluating neoplasia of a colorectal tissue, comprising at least 2 probes according to claim 16.
- 10 19. The diagnostic reagent of claim 18 which comprises at least 5 probes according to claim 16.
20. The diagnostic reagent of claim 18 which comprises at least 10 probes according to claim 16.
- 15 21. The diagnostic reagent of claim 18 which comprises at least 20 probes according to claim 16.
22. The diagnostic reagent of claim 18 which comprises at least 30 probes according to claim 16.
23. A diagnostic reagent for evaluating neoplasia of a colorectal tissue, comprising at least 2 probes according to claim 17.
- 20 24. A method of diagnosing pancreatic cancer in a sample suspected of being neoplastic, comprising the steps of:

comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a pancreatic tissue suspected of being neoplastic and the second sample is of a normal human colon tissue, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 4;

identifying the first sample as neoplastic when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

25. A method of diagnosing cancer in a sample suspected of being neoplastic, comprising the steps of:

comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a tissue suspected of being neoplastic and the second sample is of a normal human tissue of the same tissue type, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 5;

identifying the first sample as neoplastic when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

26. A method to aid in the determination of a prognosis for a colon cancer patient, comprising the steps of:

comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic colonic tissue and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 3;

determining a poorer prognosis if the level of the at least one transcript is found to be lower in the first sample than in the second sample.

27. A method to aid in determining a prognosis for a patient with colon cancer, comprising the steps of:

comparing the level of at least one transcript in a first tissue sample to a second sample, wherein the first sample is of a colonic cancer tissue and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 2;

determining a poorer prognosis if the level of the at least one transcript is found to be higher in the first sample than in the second sample.

28. A method of diagnosing colon cancer in a sample suspected of being neoplastic, comprising the steps of:

comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 3;

identifying the first sample as neoplastic when the level of expression of the protein is found to be lower in the first sample than in the second sample.

29. A method of diagnosing colon cancer in a sample suspected of being neoplastic, comprising the steps of:

comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 2;

identifying the first sample as neoplastic when expression of the protein is found to be higher in the first sample than in the second sample.

30. A method to aid in determining a prognosis of a patient having pancreatic cancer, comprising the steps of:

5 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic pancreatic tissue and the second sample is of a normal human colon tissue, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 4;

 determining a poorer prognosis if the level of the at least one transcript is found to be higher in the first sample than in the second sample.

10 31. A method to aid in providing a prognosis for a cancer patient, comprising the steps of:

 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic tissue and the second sample is of a normal human tissue of the same tissue type, 15 wherein said transcript is identified by a tag selected from the group consisting of those shown Table 5;

 determining a poorer prognosis if the level of the at least one transcript is found to be higher in the first sample than in the second sample.

20 32. A method of diagnosing pancreatic cancer in a sample suspected of being neoplastic, comprising the steps of:

 comparing the level of expression of at least one protein encoded by a transcript in a first sample of a tissue to a second sample, wherein the first sample is of a pancreatic tissue suspected of being neoplastic and the second sample is of a normal human colon tissue, wherein said protein is 25 encoded by a transcript identified by a tag selected from the group consisting of those shown Table 4;

 identifying the first sample as neoplastic when expression of the protein is found to be higher in the first sample than in the second sample.

33. A method of diagnosing cancer in a sample suspected of being neoplastic, comprising the steps of:

5 comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a tissue suspected of being neoplastic and the second sample is of a normal human tissue, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 5;

 identifying the first sample as neoplastic when expression of the protein is found to be higher in the first sample than in the second sample.

10 34. A method to aid in the determination of a prognosis for a colon cancer patient, comprising the steps of:

 comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic colonic tissue and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 3;

15 determining a poorer prognosis if the level of expression is found to be lower in the first sample than in the second sample.

20 35. A method to aid in determining a prognosis for a patient with colon cancer, comprising the steps of:

 comparing the level of expression of at least one protein in a first tissue sample to a second sample, wherein the first sample is of a colonic cancer tissue and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 2;

25 determining a poorer prognosis if the level of expression is found to be higher in the first sample than in the second sample.



36. A method to aid in determining a prognosis of a patient having pancreatic cancer, comprising the steps of:

5 comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic pancreatic tissue and the second sample is of a normal human colon tissue, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 4;

 determining a poorer prognosis if the level of expression is found to be higher in the first sample than in the second sample.

10 37. A method to aid in providing a prognosis for a cancer patient, comprising the steps of:

 comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic tissue and the second sample is of a normal human tissue of the same
15 tissue type, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 5;

 determining a poorer prognosis if the level of expression is found to be higher in the first sample than in the second sample.

20 38. A method of treating a cancer cell, comprising the step of:

 administering to a cancer cell an antibody which specifically binds to a protein encoded by a transcript identified by a tag selected from the group consisting of those shown in Tables 2, 4, and 5, wherein the antibody is linked to a cytotoxic agent.

25 39. An antibody linked to a cytotoxic agent, wherein the antibody specifically binds to a protein encoded by a transcript identified by a tag selected from the group consisting of those shown in Tables 2, 4, and 5.

40. A method of detecting colon cancer in a patient, comprising the steps of:

5 comparing the level of at least one protein in a first body sample to a second body sample, wherein the first sample is a body sample of the patient and the second sample is of a normal human, wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 2, wherein the first and second body sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

10 identifying neoplasia when the level of the at least one protein is found to be higher in the first sample than in the second sample.

41. A method of detecting pancreatic cancer in a patient, comprising the steps of:

15 comparing the level of at least one protein encoded by a transcript in a first sample of a tissue to a second sample, wherein the first sample is of the patient and the second sample is of a normal human, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 4, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

20 identifying neoplasia when the level of the at least one protein is found to be higher in the first sample than in the second sample.

42. A method of detecting cancer in a patient, comprising the steps of:

25 comparing the level of at least one protein in a first sample to a second sample, wherein the first sample is of patient and the second sample is of a normal human, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 5, wherein the first and second body sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

identifying neoplasia when the level of the at least one protein is found to be higher in the first sample than in the second sample.

43. A method to aid in determining a prognosis for a patient with colon cancer, comprising the steps of:

5 comparing the level of at least one protein in a first sample to a second sample, wherein the first sample is of a colonic cancer patient and the second sample is of a normal human, wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 2, wherein the first and second sample is a sample selected from the
10 group consisting of blood, urine, feces, sputum, and serum;

 determining a poorer prognosis if the level of the at least one protein is found to be higher in the first sample than in the second sample.

44. A method to aid in determining a prognosis of a patient having pancreatic cancer, comprising the steps of:

15 comparing the level of at least one protein in a first sample to a second sample, wherein the first sample is of a pancreatic cancer patient and the second sample is of a normal human, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 4, wherein said first and second sample is a sample selected from the
20 group consisting of blood, urine, feces, sputum, and serum;

 determining a poorer prognosis if the level of the at least one protein is found to be higher in the first sample than in the second sample.

45. A method to aid in providing a prognosis for a cancer patient, comprising the steps of:

25 comparing the level of expression of at least one protein in a first sample to a second sample, wherein the first sample is of a cancer patient and the second sample is of a normal human, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those

shown Table 5, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

determining a poorer prognosis if the level of the at least one protein is found to be higher in the first sample than in the second sample.

- 5 46. A method of detecting colon cancer in a patient, comprising the steps of:

 comparing the level of at least one transcript in a first body sample to a second body sample, wherein the first sample is a body sample of the patient and the second sample is of a normal human, wherein the transcript
10 is identified by a tag selected from the group consisting of those shown in Table 2, wherein the first and second body sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

 identifying neoplasia when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

- 15 47. A method of detecting pancreatic cancer in a patient, comprising the steps of:

 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of the patient and the second sample is of a normal human, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 4, wherein the
20 first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

 identifying neoplasia when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

- 25 48. A method of detecting cancer in a patient, comprising the steps of:

 comparing the level of at least one transcript in a first sample to a second sample, wherein the first sample is of patient and the second sample is of a normal human, wherein said transcript is identified by a tag selected

from the group consisting of those shown Table 5, wherein the first and second body sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

5 identifying neoplasia when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

49. A method to aid in determining a prognosis for a patient with colon cancer, comprising the steps of:

10 comparing the level of at least one transcript in a first sample to a second sample, wherein the first sample is of a colonic cancer patient and the second sample is of a normal human, wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 2, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

15 determining a poorer prognosis if the level of the at least one transcript is found to be higher in the first sample than in the second sample.

50. A method to aid in determining a prognosis of a patient having pancreatic cancer, comprising the steps of:

20 comparing the level of at least one transcript in a first sample to a second sample, wherein the first sample is of a pancreatic cancer patient and the second sample is of a normal human, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 4, wherein said first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

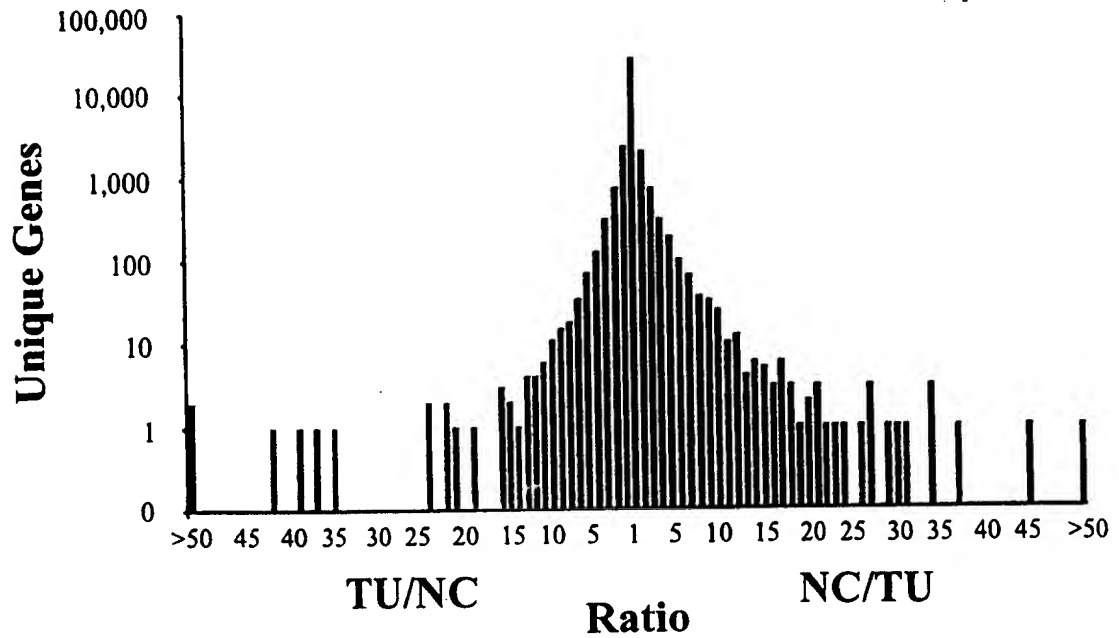
25 determining a poorer prognosis if the level of the at least one transcript is found to be higher in the first sample than in the second sample.

51. A method to aid in providing a prognosis for a cancer patient, comprising the steps of:

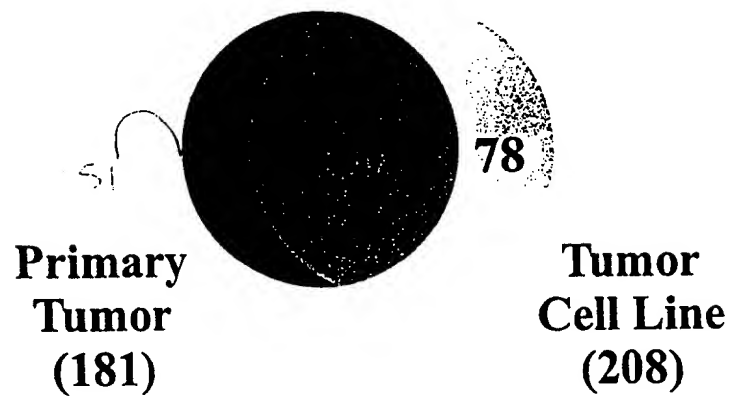
5 comparing the level of expression of at least one transcript in
a first sample to a second sample, wherein the first sample is of a cancer patient
and the second sample is of a normal human, wherein said transcript is
identified by a tag selected from the group consisting of those shown Table 5,
wherein the first and second sample is a sample selected from the group
consisting of blood, urine, feces, sputum, and serum;

 determining a poorer prognosis if the level of the at least one
transcript is found to be higher in the first sample than in the second sample.

10 52. A method for screening for candidate agents that modulate the
expression of a polynucleotide selected from the group consisting of the
polynucleotides in SEQ ID NOS:1-732 or their respective complements,
comprising contacting a test agent with a colon or pancreatic cell and
monitoring expression of the polynucleotide, wherein the test agent which
modifies the expression of the polynucleotide is a candidate agent.



B.



C.

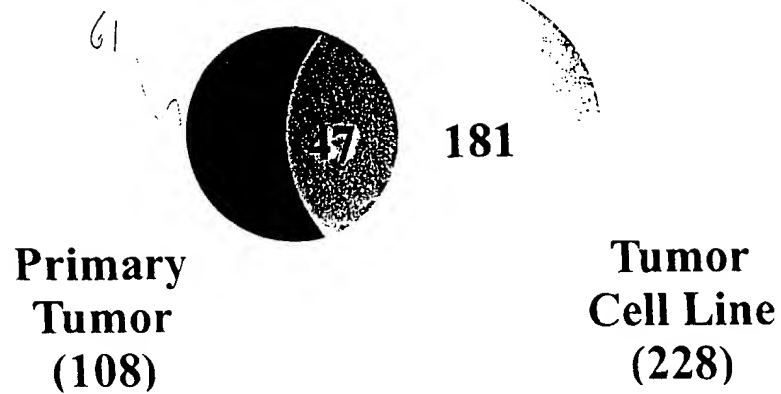
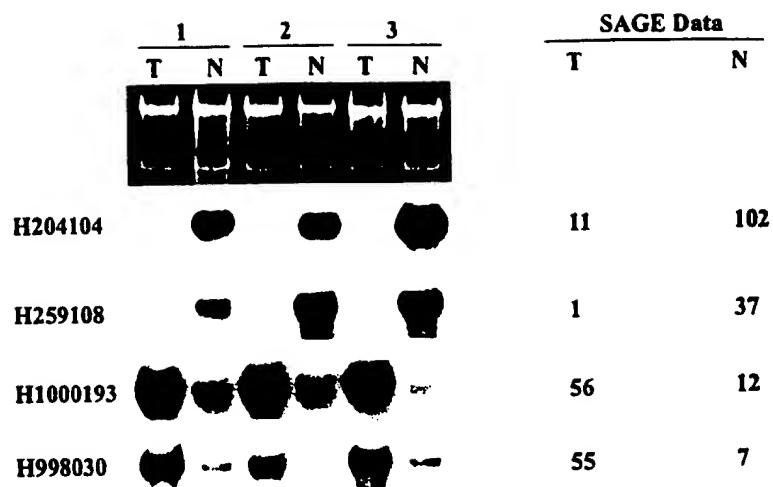
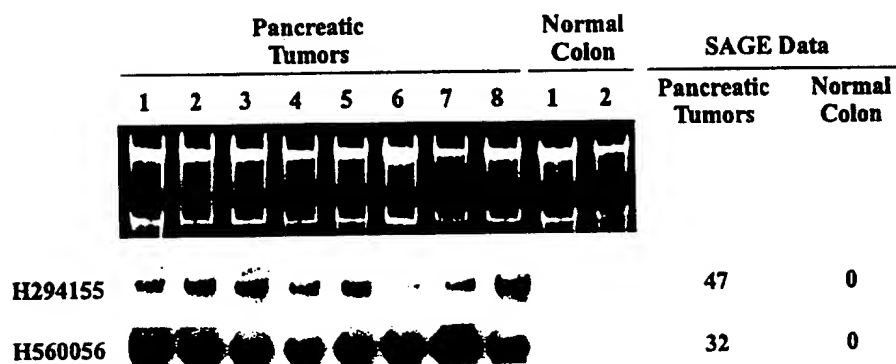


FIG. 2

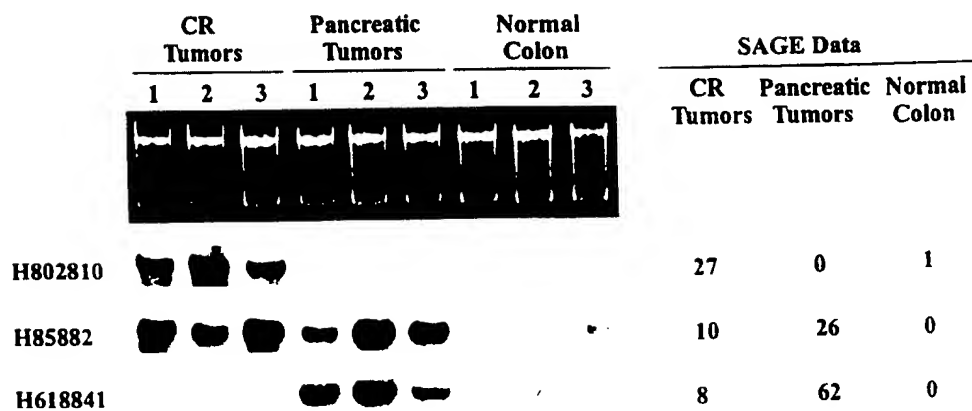
A.



B.



C.



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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C12Q 1/68, G01N 33/574	A3	(11) International Publication Number: WO 98/53319 (43) International Publication Date: 26 November 1998 (26.11.98)
(21) International Application Number: PCT/US98/10277 (22) International Filing Date: 20 May 1998 (20.05.98) (30) Priority Data: 60/047,352 21 May 1997 (21.05.97) US (63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Application US 60/047,352 (CON) Filed on 21 May 1997 (21.05.97) (71) Applicant (for all designated States except US): THE JOHNS HOPKINS UNIVERSITY [US/US]; Suite 2-100, 2024 E. Monument Street, Baltimore, MD 21205 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): VOGELSTEIN, Bert [US/US]; The Johns Hopkins University, Suite 2-100, 2024 E. Monument Street, Baltimore, MD 21205 (US). KINZLER, Kenneth, W. [US/US]; The Johns Hopkins University, Suite 2-100, 2024 E. Monument Street, Baltimore, MD 21205 (US).		(74) Agents: KAGAN, Sarah, A. et al.; Banner & Witcoff, Ltd., 11th floor, 1001 G Street, N.W., Washington, DC 20001-4597 (US). (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 8 July 1999 (08.07.99)
(54) Title: GENE EXPRESSION PROFILES IN NORMAL AND CANCER CELLS (57) Abstract As a step towards understanding the complex differences between normal and cancer cells, gene expression patterns were examined in gastrointestinal tumors. More than 300,000 transcripts derived from at least 45,000 different genes were analyzed. Although extensive similarity was noted between the expression profiles, more than 500 transcripts that were expressed at significantly different levels in normal and neoplastic cells were identified. These data provide insights into the extent of expression differences underlying malignancy and reveal genes that are useful as diagnostic or prognostic markers.		

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INTERNATIONAL SEARCH REPORT

International Application No

PL JS 98/10277

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12Q1/68 G01N33/574

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12Q G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SUGIO K ET AL.: "Differential expression of c-myc gene and c-fos gene in premalignant and malignant tissues." CANCER RESEARCH, vol. 48, no. 17, 1988, pages 4855-4861, XP002089885 see the whole document	1,3,13, 16,17,28
X	VAN BELZEN N ET AL.: "Detection of different gene expression in differentiating colon carcinoma cells by differential display" JOURNAL OF PATHOLOGY, vol. 178, no. Suppl., - 1996 page 2A XP002089886	1,3,5,7, 9,11
Y	see abstract	26,28,34



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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- "O" document referring to an oral disclosure, use, exhibition or other means
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Date of the actual completion of the international search

13 January 1999

Date of mailing of the international search report

24.05.1999

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Knehr, M

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 98/10277

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 95 21944 A (SMITHKLINE BEECHAM CORP ;ROSENBERG MARTIN (US); DEBOUCK CHRISTINE) 17 August 1995 see the whole document ---	26,28,34
Y	EP 0 284 362 A (ICI PLC) 28 September 1988 see abstract see page 2, line 44 - line 51 see page 10, line 12 - line 15; claims 1,9; figure 2 ---	1,3,5,7, 9,11, 13-23, 26,28, 34,52
Y	EP 0 761 822 A (UNIV JOHNS HOPKINS MED) 12 March 1997 see the whole document ---	1,3,5,7, 9,11, 13-23, 26,28, 34,52
Y	WO 95 11923 A (DANA FARBER CANCER INST INC ;CHEN LAN BO (US); BAO SHIDENG (CN); L) 4 May 1995 see the whole document ---	1,3,5,7, 9,11, 13-18, 23,26, 28,34,52
Y	VELCULESCU V E ET AL: "SERIAL ANALYSIS OF GENE EXPRESSION" SCIENCE, vol. 270, 20 October 1995, pages 484-487, XP002053721 cited in the application see the whole document ---	1,3,5,7, 9,11, 13-18, 23,26, 28,34,52
Y	SCHWEINFEST C W ET AL.: "Subtraction hybridization cDNA libraries from colon carcinoma and hepatic cancer" GENETIC ANALYSIS TECHNIQUES AND APPLICATIONS, vol. 7, 1990, pages 64-70, XP002089887 see the whole document ---	1,3,5,7, 9,11, 13-18, 23,26
Y	WO 97 14812 A (CHIRON CORP) 24 April 1997 see the whole document ---	52
A	GRESS T M ET AL.: "A pancreatic cancer-specific expression profile" ONCOGENE, vol. 13, 1996, pages 1819-1830, XP002089888 see the whole document ---	

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INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 98/10277

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 95 19369 A (UNIV VANDERBILT) 20 July 1995 see the whole document ---	
A	GRESS T ET AL.: "Identification of genes with pancreatic cancer specific expression by use of cDNA representational difference analysis" GASTROENTEROLOGY, vol. 110, no. 4 Suppl., 1996, XP002089889 see abstract ---	
P,X	ZHANG L E AL.: "Gene expression profiles in normal and cancer cells." SCIENCE, vol. 276, 1997, pages 1268-1272, XP002089890 see the whole document ---	1,3,5,7, 9,11, 13-23, 26,28, 34,52
P,X	VAN BELZEN N ET AL.: "A novel gene which is up-regulated during colon epithelial cell differentiation and down-regulated in colorectal neoplasms" LABORATORY INVESTIGATION, vol. 77, no. 1, 1997, pages 85-92, XP002089891 see the whole document -----	1,3,5,7, 9,11,13, 14, 16-18, 23,26, 28,34

Form PCT/ISA/210 (continuation of second sheet) (22)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 98/ 10277

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see FURTHER INFORMATION sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see FURTHER INFORMATION sheet, subject 1.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/ US 98/10277

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1,3,5,7,9,11,13-23,26,28,34,52 (partial)

INVENTION 1:

An isolated and purified human nucleic acid molecule comprising SEQ ID NO:291 of table 3 (INVENTION 1), an isolated nucleotide probe hybridizing to it, a diagnostic reagent comprising at least two of such probes, methods of diagnosing or prognosing colon cancer using them, and a method for screening for agents modulating the expression of such a sequence using them.

2. Claims: 1,3,5,7,9,11,13-23,26,28,34,52 (partial)

INVENTION 2 to INVENTION 259:

An isolated and purified human nucleic acid molecule comprising SEQ ID NO:292 of table 3 (INVENTION 2), an isolated nucleotide probe hybridizing to it, a diagnostic reagent comprising at least two of such probes, methods of diagnosing or prognosing colon cancer using them, and a method for screening for agents modulating the expression of such a sequence using them.

...ibidem for each of the SEQ ID Nos:293 to 549 (INVENTION 3 to INVENTION 259) as specified in table 3, separately.

3. Claims: 2,4,6,8,10,12-23,27,29,35,38-40,43,46,49, 52 (partial)

INVENTION 260 to INVENTION 549:

An isolated and purified human nucleic acid molecule comprising SEQ ID NO:1 of table 2 (INVENTION 260), an isolated nucleotide probe hybridizing to it, a diagnostic reagent comprising at least two of such probes, methods of diagnosing or prognosing colon cancer using them, a method of treating a cancer cell using them, an antibody linked to a cytotoxic agent used in such a method, and a method for screening for agents modulating the expression of such a sequence using them.

...ibidem for each of the SEQ ID Nos:2 to 290 (INVENTION 261 to INVENTION 549) as specified in table 2, separately.

4. Claims: 13-24,30,32,36,38,39,41,44,47,50,52 (partial)

INTERNATIONAL SEARCH REPORT

International Application No. PCT/ US 98/10277

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

INVENTION 550 to INVENTION 732:

An isolated and purified human nucleic acid molecule comprising SEQ ID NO:550 of table 4 (INVENTION 550), an isolated nucleotide probe hybridizing to it, a diagnostic reagent comprising at least two of such probes, methods of diagnosing or prognosing pancreatic cancer using them, a method of treating a cancer cell using them, an antibody linked to a cytotoxic agent used in such a method, and a method for screening for agents modulating the expression of such a sequence using them.

...ibidem for each of the SEQ ID Nos:551 to 732 (INVENTION 551 to INVENTION 732) as specified in table 4, separately.

5. Claims: 24,30,32,36,38,39,41,44,47,50 (partial)

INVENTION 733 to INVENTION 734:

Methods of diagnosing or prognosing pancreatic cancer relying on a human nucleic acid molecule comprising SEQ ID NO:733 of table 4 (INVENTION 733), a method of treating a cancer cell using it, and an antibody linked to a cytotoxic agent used in such a method.

...ibidem for SEQ ID Nos:734 (INVENTION 734) as specified in table 4.

6. Claims: 25,31,33,37-39,42,45,48,51 (partial)

INVENTION 735 to INVENTION 870:

Methods of diagnosing or prognosing cancer relying on a human nucleic acid molecule comprising SEQ ID NO:735 of table 5 (INVENTION 735), a method of treating a cancer cell using it, and an antibody linked to a cytotoxic agent used in such a method.

...ibidem for each of the SEQ ID Nos:736 to 870 (INVENTION 736 to INVENTION 870) as specified in table 5, separately.

INTERNATIONAL SEARCH REPORT

.ormati patent family members

Inte. Application No

PCT/US 98/10277

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9521944 A	17-08-1995	EP 0743989 A JP 9508800 T	27-11-1996 09-09-1997
EP 0284362 A	28-09-1988	AU 625169 B AU 1337888 A DK 159788 A FI 881388 A JP 1034291 A PT 87055 A,B	02-07-1992 22-09-1988 24-09-1988 24-09-1988 03-02-1989 01-04-1988
EP 0761822 A	12-03-1997	US 5695937 A US 5866330 A AU 6561496 A AU 7018896 A CA 2185379 A GB 2305241 A IE 80465 B JP 10511002 T WO 9710363 A	09-12-1997 02-02-1999 20-03-1997 01-04-1997 13-03-1997 02-04-1997 12-08-1998 27-10-1998 20-03-1999
WO 9511923 A	04-05-1995	CA 2175380 A EP 0725799 A US 5889159 A US 5872235 A	04-05-1995 14-08-1996 30-03-1999 16-02-1999
WO 9714812 A	24-04-1997	AU 7264196 A EP 0862651 A	07-05-1997 09-09-1998
WO 9519369 A	20-07-1995	US 5677125 A AU 1831795 A CA 2210396 A EP 0804453 A	14-10-1997 01-08-1995 20-07-1995 05-11-1997